Complete Summary

GUIDELINE TITLE

VHA/DOD clinical practice guideline for the management of chronic obstructive pulmonary disease.

BIBLIOGRAPHIC SOURCE(S)

Veterans Health Administration (VHA). Clinical practice guideline for the management of chronic obstructive pulmonary disease. Version 1.1a. Washington (DC): Department of Veterans Affairs (U.S.), Veterans Health Administration; 1999 Aug. 116 p.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Chronic Obstructive Pulmonary Disease (COPD)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Emergency Medicine
Internal Medicine
Pulmonary Medicine

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians
Respiratory Care Practitioners

GUIDELINE OBJECTIVE(S)

- To assist primary care providers or specialists in the early detection of symptoms, assessment of the clinical situation, determination of appropriate treatment, and delivery of individualized interventions
- To provide enough guidance for a broad range of clinical settings, while at the same time providing enough flexibility to accommodate local practice and individual situations
- To promote evidence-based management of persons with chronic obstructive pulmonary disease (COPD) and thereby improve clinical outcomes

TARGET POPULATION

Veterans with chronic obstructive pulmonary disease (COPD)

INTERVENTIONS AND PRACTICES CONSIDERED

Outpatient management of chronic obstructive pulmonary disease (COPD)

1. Clinical assessment:
    - History: including smoking status, activity level, exercise tolerance
    - Physical exam: including assessment of airflow obstruction
    - Laboratory tests: including spirometry, chest x-ray, oximetry, alpha1-antitrypsin level
2. Evaluate for acute and/or severe exacerbation
3. Pre- and postbronchodilation spirometry
4. Pharmacotherapy
    - Inhaled anticholinergic therapy (ipratropium)
    - Long-acting inhaled beta2-agonists (LAIBA) (salmeterol)
    - Short-acting inhaled beta2-agonists (SAIBA) (albuterol, metaproterenol, terbutaline)
    - Combination therapy with inhaled anticholinergics and short acting beta2-agonists
    - Inhaled medication using metered dose inhaler (MDI) or nebulizer (NEB)
    - Systemic corticosteroid therapy (prednisone)
    - Theophylline trial
    - Theophylline combination therapy
    - Antibiotic therapy for concurrent respiratory infection (sulfamethoxazole-trimethoprim [SMZ-TMP], doxycycline)
5. Long-term oxygen therapy
6. Preoperative evaluation and management, including pulmonary function tests, arterial blood gases, counseling on smoking cessation; postoperative management, including subcutaneous heparin
7. Air travel management, including oxygen supplementation
8. Insomnia, including:

- Education on proper sleep hygiene
- Hypnotics (benzodiazepines, zolpidem, triazolam)

Inpatient Management of Chronic Obstructive Pulmonary Disease

1. Emergency department (cardiopulmonary resuscitation, mechanical ventilation)
2. Clinical and laboratory evaluation
3. Intensive care unit or hospital ward admission
4. Pharmacotherapy
    - Anticholinergics (ipratropium bromide)
    - Short-acting inhaled beta2-agonists (SAIBA) (albuterol, metaproterenol, terbutaline)
    - Theophylline
    - Systemic steroids (solumedrol, prednisone, prednisilone)
    - Antibiotics
5. Oxygen therapy

MAJOR OUTCOMES CONSIDERED

- Change in pulmonary function (FEV_1 - peak expiratory flow rate)
- Symptom control

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The algorithms and annotations contained in this guideline are based in part on the chronic obstructive pulmonary disease (COPD) guidelines developed in 1997. Additional literature related to the population being studied (adults) and the treatment setting (primary care) was provided on an ad hoc basis by Birch and Davis Associates, Inc. (the subcontractor) to supplement the original search. The original search was conducted in Medline (U.S. National Library of Medicine).

The Medical Subject Headings (MeSH) include: Diseases; Respiratory Tract Diseases; Lung Diseases; Lung Diseases-Obstructive; Atelectasis; Bronchopulmonary Dysplasia; Asthma; Bronchitis; Pulmonary Emphysema. Selection of articles was then based on key therapies in chronic obstructive pulmonary disease (COPD), study characteristics, and study design. In this search, "study characteristics" are those of analytic studies, case-control studies, retrospective studies, cohort studies, longitudinal studies, follow-up studies, prospective studies, cross-sectional studies, clinical protocols, controlled clinical trials, randomized clinical trials (RCTs), intervention studies, and sampling studies. Study design includes crossover studies, double-blind studies, matched pair analysis, meta-analysis, random allocation, reproducibility of results, and sample size.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Level of Evidence Grading: Primary (Secondary)

A. Randomized clinical trials (Other clinical studies)
B. Well-designed clinical studies (Clinical studies related to topic but not in this clinical population)
C. Panel consensus (Clinical studies related to topic but not in this clinical population)

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not applicable

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The guideline recommendations are the product of many months of consensus building among knowledgeable individuals, including private sector experts provided by the contractor, the Veterans Health Administration and Department of Defense professionals from across the health care continuum.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of Recommendation Grading

Grade I: Usually indicated, always acceptable, and considered useful and effective.

Grade IIa: Acceptable, of uncertain effectiveness, and may be controversial. Weight of evidence in favor of usefulness/effectiveness.

Grade IIb: Acceptable, of uncertain effectiveness, and may be controversial. Not well established by evidence, can be helpful, and probably not harmful.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not applicable

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The recommendations for the management of chronic obstructive pulmonary disease are organized into 2 major sections: outpatient management and inpatient management. The first section contains 7 algorithms and the second section contains 3 algorithms. Each algorithm, the annotations that accompany it, and the evidence supporting the recommendations are presented below. The strength of recommendation grading (I-IIb) and level of evidence grading (A-C) are defined following the "Major Recommendations".

Note: A list of all abbreviations is provided at the end of the "Major Recommendations" field.

Core Module

Outpatient Management of Chronic Obstructive Pulmonary Disease (COPD) (Core Algorithm)

A. Patient with Suspected or Confirmed Chronic Obstructive Pulmonary Disease Presents to Primary Care

Definitions

1. Chronic obstructive pulmonary disease (COPD) is a disorder characterized by the presence of airflow obstruction due to chronic bronchitis or emphysema; the airflow obstruction is generally slowly progressive, may be accompanied by airway hyperactivity, and may be partially reversible.
2. Chronic bronchitis is defined as the presence of chronic productive cough for 3 months of each of two successive years in a patient in whom other causes of chronic cough have been excluded (asthma, post nasal discharge, gastroesophageal reflux disease [GERD], etc.).

3. Emphysema is defined as abnormal permanent enlargement of the air spaces distal to the terminal bronchioles, accompanied by destruction of their walls and without obvious fibrosis.
4. Asthma is by definition associated with reversible airflow obstruction. Patients with asthma whose airflow obstruction is completely reversible are not considered to have COPD. The obstruction in many patients with COPD may include a significant reversible component. Some patients with asthma may develop irreversible airflow obstruction indistinguishable from COPD.

Evidence

Definition of COPD: Level of Evidence: C; Strength of Recommendation: IIa (American Thoracic Society [ATS], 1991, 1995; Siafakas, 1995; British Thoracic Society [BTS], 1997).

B. Perform Clinical Assessment, History, Physical Examination, Laboratory Tests

Objective

To collect information needed to assess the patient.

Annotation

1. History
    a. Smoking: Age at initiation, quantity smoked per day, whether or not still smoker and if not, date of cessation
    b. Environmental (chronological), e.g., dust exposure (may disclose important risk factors)
    c. Cough (chronic, productive): Frequency and duration, whether or not productive (especially on awakening)
    d. Wheezing
    e. Acute chest illnesses: Frequency, productive cough, wheezing, dyspnea, fever
    f. Dyspnea
    g. Evaluate current therapy
2. Physical examination of chest
    a. Airflow obstruction evidenced by:
        - Wheezing during auscultation on slow or forced breathing
        - Forced expiratory time of more than 6 seconds
    b. Severe emphysema indicated by:
        - Overdistention of lungs in stable state, low diaphragmatic position
        - Decreased intensity of breath and heart sounds
    c. Severe disease suggested by (characteristics not diagnostic):
        - Pursed-lip breathing
        - Use of accessory respiratory muscles
        - Indrawing of lower interspaces
    d. Other: Unusual positions to relieve dyspnea at rest, digital clubbing (suggests possibility of lung cancer or bronchiectasis),

and mild dependent edema that may be seen in absence of right heart failure.

3. Laboratory
    a. Spirometry: FEV_1 (forced expiratory volume in one second) and VC (vital capacity)
    b. Chest radiography: Diagnostic only of severe emphysema but essential to exclude other lung diseases.
    c. Oximetry should be done to help determine if there is a need for oxygen therapy. It may be done at this time or at the time of applying the long-term oxygen therapy (see module A3).
    d. Alpha1-antitrypsin (AAT): AAT deficiency accounts for less than one percent of COPD. If AAT deficiency is suspected, obtain a serum AAT level. Strongly consider referral to specialist in the following situations:
        - Premature onset of COPD with moderate or severe impairment before age 50
        - A predominance of basilar emphysema; development of unremitting asthma, especially in a patient under age 50
        - A family history of AAT deficiency or of COPD onset before age 50
        - Chronic bronchitis with airflow obstruction in a person who has never smoked
        - Bronchiectasis, especially in the absence of clear risk factors for the disease
        - Cirrhosis in a patient without apparent risk factors. If diagnosis of COPD or asthma is made, refer to specialist for recommendations for therapy

Evidence

Clinical and laboratory evaluation: Level of Evidence: C; Strength of Recommendation: IIa (ATS, 1995; Siafakas, 1995; BTS, 1997).

C. Is Patient in Acute Exacerbation?

Objective

To identify patients in an acute exacerbation.

Annotation

An acute exacerbation of COPD is defined as an acute clinical deterioration in a patient's respiratory status due to a worsening of the underlying COPD. Symptoms and signs of acute exacerbation of COPD may include:

1. Increased dyspnea
2. Tachycardia
3. Increased cough
4. Increased sputum production
5. Change in sputum color or character
6. Accessory muscle use
7. Peripheral edema

8. Development of or increase in wheeze
9. Loss of alertness
10. Loss of energy
11. Fever
12. Increased respiratory rate
13. Decrease in FEV_1 or peak expiratory flow
14. Worsening of arterial blood gases or pulse oximetry
15. Chest tightness

Evidence

Definition of acute exacerbation: Level of Evidence: C; Strength of Recommendation: IIa (Siafakas, 1995; BTS, 1997).

D. Is there Evidence of Severe Exacerbation?

Objective

To identify patients with a severe exacerbation that requires emergency room care.

Annotation

Loss of alertness or a combination of two or more of the following parameters indicate a severe exacerbation and suggest a need for referral to an emergency department.

1. Dyspnea at rest
2. Respiratory rate $\geq$ 25 per minute
3. Heart rate $\geq$ 110 per minute
4. Use of accessory muscles

Evidence

Severity of exacerbation: Level of Evidence: C; Strength of Recommendation: IIa (Siafakas, 1995).

E. Order/Review Spirometry

Objective

To objectively assess pulmonary function in patients with COPD.

Annotation

On initial visit:

Spirometry pre- and postbronchodilation are essential to confirm presence and reversibility of airflow obstruction and to quantify maximum level of ventilatory function, guide management, and estimate prognosis.

On follow up visits:

Repeat spirometry if major change in patient's condition. On new patients previous spirometry may be used if available and no change in patient's condition.

1. Airflow limitation is diagnosed by a reduction in FEV_1/VC
2. Lung volumes: Unnecessary except in special circumstances (e.g., coexisting interstitial lung disease, presence of giant bullae, and decrease in VC)
3. Carbon monoxide diffusing capacity: Unnecessary except in special instances (e.g., dyspnea out of proportion to severity of airflow limitation)

Evidence

Interpretation of pulmonary function: Level of Evidence: C; Strength of Recommendation: IIa (ATS, 1995; Siafakas, 1995; BTS, 1997).

F. Initiate/Adjust Pharmacological Therapy

Objective

To determine the appropriate therapy based on severity of symptoms.

Annotation

Table. Step Care In Chronic Obstructive Pulmonary Disease

Step	Symptoms and FEV_1	Therapy
1	Asymptomatic AND FEV_1 > 50 percent of predicted (1)	Smoking cessation, vaccination, employ education. No medication indicated.
2a	Symptoms less than daily AND $FEV_1 \geq$ 50 percent of predicted (2)	Smoking cessation, vaccination, employ education. Inhaled short-acting beta2-agonist (2 puffs PRN up to 12 puffs/day)
2b	Asymptomatic AND FEV_1 < 50 percent of predicted	Smoking cessation, vaccination, employ education. Inhaled anticholinergic (2 puffs q.i.d) Consider use of inhaler containing a short acting beta2-agonist and an anticholinergic.
2c	Symptoms less than daily AND	Smoking cessation, vaccination, employ education. Inhaled

	FEV_1 < 50 percent of predicted OR Daily symptoms	anticholinergic (2 puffs q.i.d) Short-acting beta2 agonist (2 puffs PRN up to 12 puffs/day) Consider use of inhaler containing a short acting beta2-agonist and an anticholinergic.
3	Symptoms not controlled (2)	Increase dose of both: Inhaled anticholinergic (2 to 6 puffs q.i.d) and inhaled short-acting beta2-agonist (2 -4 puffs PRN up to 12 puffs/day)
4	Symptoms not controlled (2)	Consider adding long-acting inhaled beta2-agonist. (3)
5	Symptoms not controlled (2)	Consider adding theophylline trial (slow release theophylline adjusted to level of 5 to 12 micrograms/ml) (4)
6	Symptoms not controlled (2)	Consider adding corticosteroid trial (prednisone 40 to 60 mg po qd or high dose inhaled steroids (5). Consider specialist consultation.
7	Symptoms not controlled (2)	Refer to specialist promptly.

1. Spirometry is essential to confirm the presence of airflow obstruction (low FEV_1 and FEV_1/VC ratio). Base therapy on symptoms, but consider alternate diagnoses (heart disease, pulmonary emboli, etc.) if out of proportion to spirometry.
2. Use the lowest level of therapy that satisfactorily relieves symptoms and maximizes activity level. Assure compliance and proper use of medications before escalating therapy.
3. Inhaled long acting beta2-agonists should not be used as rescue therapy. Short-acting inhaled beta2-agonist (less than 12 puffs/day) may continue to be used PRN. Nighttime symptoms are frequently better controlled with long-acting inhaled beta2-agonist. Oral beta2-agonists are associated with a higher rate of side effects, and should be reserved for patients who cannot take inhaled beta2-agonist medications.
4. Theophylline should be used with caution because of potential for severe side effects. Nighttime respiratory symptoms are frequently controlled but theophylline may lead to insomnia. Theophylline should be discontinued if a symptomatic or objective benefit is not evident within several weeks.

5. A corticosteroid trial of prednisone (40 to 60mg/day) 10 to14 days, or high dose inhaled steroids (equivalent to 880 micrograms or more of fluticasone or 800 micrograms or more of budesonide) of 14 to 21 days can help identify patients who may benefit from long term steroid use. Responders to oral steroids should transition to the lowest effective dose of inhaled steroids, or to the lowest effective dose of a combination of inhaled and oral steroids, if possible, to avoid the long term complications of systemic corticosteroids. If oral steroids are used other than for an acute exacerbation, obtain spirometry prior to and after trial to confirm an objective response.

G. Apply Long-Term Oxygen Therapy

Objective

To maintain an acceptable level of O_2 saturation and improve survival.

Annotation

In COPD patients with hypoxemia and cor pulmonale, treatment with long-term oxygen therapy (LTOT) may increase the life span by six to seven years. Mortality is reduced in patients with chronic hypoxemia when oxygen is administered for more than 12 hours daily and greater survival benefits have been shown with continuous oxygen administration. See Module A3, Long-term Oxygen Therapy for details and references.

H. Is There Evidence of Cardiac Disease?

Objective

To identify patients with symptomatic left ventricular heart disease.

Annotation

Cardiac disease from systolic or diastolic left ventricular dysfunction leading to pulmonary edema can produce symptoms similar to that of COPD, namely dyspnea, wheezing, tachycardia, chest discomfort, orthopnea, paroxysmal nocturnal dyspnea. A history of coronary artery disease, hypertension, or cardiomyopathy should prompt further evaluation or treatment modifications.

I. Are There Symptoms of Sleep Apnea?

Objective

To identify patients who may benefit from treatment by a sleep disorder specialist.

Annotation

Some signs and symptoms of COPD, including hypercapnia, are precipitated by sleep apnea. Major symptoms of sleep apnea include:

1. Excessive daytime sleepiness (EDS)
2. Heavy snoring
3. Observed apnea during sleep
4. Choking during sleep

Evidence

COPD patients do not normally have EDS, even with nocturnal desaturation: Level of Evidence: C; Strength of Recommendation: IIa (Orr, 1990).

COPD patients with obstructive sleep apnea are likely to have day time hypercapnia: Level of Evidence: C; Strength of Recommendation: IIa (Bradley, 1990).

J. Patient Complains of Insomnia?

Objective

To identify patients who may benefit from treatment of insomnia.

Annotation

Insomnia is defined as an inability to initiate or maintain sleep to the patient's satisfaction plus a deleterious subjective or objective effect on daytime activities. Medications, such as beta2-agonists, theophylline and steroids, can produce insomnia. See Insomnia Module A6.

K. Initiate/Continue Preventive Care and Patient Education

Objective

To initiate and optimize preventive care and patient education for COPD.

Annotation

The main items in COPD patient education are:

1. Smoking Cessation
   All smokers should be strongly advised to quit. Smoking cessation results in a small improvement in lung function and a slowing of the rate of decline to approximately that seen in never smokers of the same age. Patients not willing to quit should receive motivational intervention to promote subsequent quitting attempts. The smoker willing to make a quit attempt should be assisted by being asked to set a quit date, providing self-help materials, encouraging nicotine replacement therapy, and referring to intensive treatments when appropriate. All patients attempting to quit should have follow-up contact scheduled. For additional details, see VHA/DoD CPG for Tobacco Use Cessation, and the U.S. Department of Health and Human Services (DHHS) Guidelines on Smoking Cessation.
2. Medication and delivery system training

3. Exercise and nutritional counseling
   A well-rounded program should include good dietary habits and encourage adjustment of weight to approximate ideal body weight. If malnourished, attempts should be made to restore nutritional balance with several small meals a day to help maintain caloric needs but avoid undue dyspnea. Forced nutrition or special diets are not recommended.
4. Immunizations
   The Advisory Committee on Immunization Practices (U.S. Centers for Disease Control and Prevention) recommends pneumococcal vaccination for all patients with COPD. They recommend that patients age 65 or older that were vaccinated more than five years previously should be revaccinated. When the status of previous vaccination is unsure, vaccination is indicated. However, the evidence for the efficacy of pneumococcal vaccination in patients with COPD is inconclusive. One small, randomized controlled trial failed to demonstrate vaccine efficacy for pneumococcal infection-related or other medical outcomes in the heterogeneous group of subjects labeled as high-risk. Case-controlled trials suggest an effectiveness of 65 to 84 percent among high-risk patients including those with COPD.
   An annual influenza vaccination is recommended for individuals with chronic pulmonary disease unless contraindicated due to severe anaphylactic hypersensitivity to egg protein. Influenza vaccination has been shown to be 30 to 80 percent effective in preventing illness, complications, and death in high-risk populations. Pneumococcal and influenza vaccines can be administered concurrently at different sites without increasing side effects.
5. Management of environment
6. Patients with COPD should avoid environmental exposures that exacerbate their symptoms (e.g., occupational exposures, second-hand smoke, and air and dust pollution) or results in respiratory infections.
7. Self-assessment and self-management
   Pulmonary Rehabilitation: Referral is indicated in patients on optimal medical therapy and who:
   a. Continue to display moderate to severe respiratory symptoms, including dyspnea
   b. Have had several emergency room or hospital admissions per year
   c. Exhibit limited functional status, restricting activities of daily living
   d. Experience impairment in quality of life
8. Occupational disabilities
9. Sexual function

Evidence

Pneumococcal vaccination: Most studies show an advantage, but one small randomized, placebo-controlled trial did not. Level of Evidence: C; Strength of Recommendation: I (BTS, 1997; CDC ACIP, 1997; Fine, 1994; Shapiro, 1984, 1991; Farr, 1995; Sims, 1988; Forrester, 1987; Simberkoff, 1986).

Annual influenza vaccination: Level of Evidence: C; Strength of Recommendation: I (CDC ACIP, 1997; BTS, 1997; Govaert, 1994; Nichol, 1994; Gross, 1988; Fedson, 1993; Foster, 1992).

Smoking cessation slows lung function decline: Level of Evidence: A; Strength of Recommendation: I (Anthonisen, 1994; BTS, 1997; Xu, 1992; Camilli, 1987; Fletcher, 1977).

Nutritional counseling: Level of Evidence: C; Strength of Recommendation: IIb (ATS, 1995; BTS, 1997; Wilson, 1986).

Pulmonary rehabilitation: Level of Evidence: C; Strength of Recommendation: IIa (ATS, 1995; Goldstein, 1994; BTS, 1997).

Occupational Disability: Level of Evidence: C; Strength of Recommendation: IIb (BTS, 1997).

L. Schedule Follow-Up

Objective

To maintain long term appropriate level of care for patients with COPD.

Annotation

For mild COPD, spirometry is the test used for measuring disease progression. As the disease becomes more severe, oximetry and ABG assume greater importance. The frequency of obtaining these measures is based on clinical symptoms and status. In general, patients with mild COPD should be seen annually; moderate COPD, six months to one year, depending upon status; and severe COPD, every six months at a minimum. Spirometry should be repeated at least every two to three years to follow the progression of disease and effects of therapy unless there is a clinically indicated reason not to do so.

Algorithm A1

Outpatient Management of COPD: Acute Exacerbation (Module A1)

A. Patient with Acute Exacerbation of COPD Presenting to Primary Care

Definition

Acute exacerbation is defined as a recent deterioration of a previously stable patient's clinical and functional state that is due to worsening of their COPD. Typical symptoms and signs of COPD exacerbation are given below.

1. Increased dyspnea
2. Tachycardia
3. Increased cough
4. Increased sputum production

5. Change in sputum color or character
6. Accessory muscle use
7. Peripheral edema
8. Development of or increase in wheeze
9. Loss of alertness
10. Loss of energy
11. Fever
12. Increased respiratory rate
13. Decrease in FEV_1 or peak expiratory flow
14. Worsening of arterial blood gases or pulse oximetry
15. Chest tightness

B. Administer Oxygen Therapy to Keep O_2 Saturation $\geq$ 90 Percent

Objective

Initiate oxygen therapy to maintain oxygen saturation $\geq$ 90 percent.

Annotation

There is not a good relationship between spirometry and blood gases in COPD exacerbation, at least in Emergency Department (ED) patients; a PaO_2 less than 60 mmHg may be found in patients with a FEV_1 up to 54 percent of normal. For that reason, O_2 saturation should be obtained for patients with mild-to-moderate COPD exacerbations.

If ambulatory facilities are available, oxygen should be given to keep O_2 saturation $\geq$ 90 percent while the patient receives more aggressive bronchodilator therapy. In some centers this may require ED management. Blood gases should be obtained to guide oxygen therapy in patients with known hypercapnea or where the status of CO_2 retention is unknown.

Patients who are stabilized after aggressive drug therapy but continue to have hypoxemia may require outpatient oxygen therapy at least on a temporary basis. Blood gases should be checked or oximetry performed in one month or soon thereafter when the patient is stable to determine the need for continued long-term oxygen therapy (LTOT).

Evidence

Benefit from oxygen therapy in COPD exacerbation: Level of Evidence: C; Strength of Recommendation: IIa (Siafakas, 1995).

Oxygen should be given when $PaO_2 \leq$ 60 mmHg, particularly in COPD with cardiac disease: Level of Evidence: C; Strength of Recommendation: I (ATS Consensus Statement, 1995).

Benefit from maintaining O_2 saturation $\geq$ 90 percent: Level of Evidence: B; Strength of Recommendation: I.

C. Is There Evidence of Respiratory Infection?

Objective

Identify the presence of a respiratory infection.

Annotation

This often is due to viral illness. In cases of bacterial infection, S. pneumoniae, H. influenzae and M. catarrhalis are frequent pathogens. Other organisms include Mycoplasma and Chlamydia.

Evidence of infection include:

1. Increased cough
2. Increase in volume and changes in the color of sputum
3. Increased shortness of breath
4. Fever

D. Consider Antibiotic Treatment

Objective

Initiate appropriate therapy for a suspected bacterial respiratory infection.

Annotation

In patients with evidence of respiratory infection, a white cell count and chest x-ray may be considered. Evidence of respiratory infection with a clear chest x-ray suggests that the exacerbation of COPD is due to purulent bronchitis. Antibiotic therapy should be considered.

Patients with a clinical presentation and chest radiograph consistent with pneumonia should be considered for admission. There are no published guidelines specifically regarding admission of COPD patients. The severity of the underlying COPD, the presence of co-morbid conditions, the judgment and reliability of the patient and caregivers, and the distance to medical care should be considered in this decision. Drug interaction should be considered if patient is under treatment with theophylline.

Evidence

Benefit from antibiotic therapy: Level of Evidence: B; Strength of Recommendation: I (Saint et al., 1995).

Benefit from antibiotic therapy prevention of further deterioration: Level of Evidence: B; Strength of Recommendation: I (Anthonisen et al., 1987).

Clinical benefit from antibiotic therapy: Level of Evidence: B; Strength of Recommendation: I (Sachs et al., 1995).

Admission should be considered for pneumonia in COPD: Level of Evidence: C; Strength of Recommendation: IIa.

E. Consider and Treat Other Factors Contributing to COPD Exacerbation

Objective

Identify and treat other factors contributing to or mimicking a COPD exacerbation.

Annotation

1. Congestive heart failure
2. Cardiac ischemia or arrhythmia
3. Drugs (hypnotics, tranquilizers, etc.)
4. Pulmonary embolism
5. Spontaneous pneumothorax
6. Inappropriate oxygen therapy
7. Metabolic diseases (diabetes mellitus, electrolyte disorders such as hypophosphatemia, hypokalemia)
8. Myopathy (e.g., steroid myopathy)
9. Other diseases (undernutrition, gastrointestinal [GI] hemorrhage, stroke, thoracic vertebral collapse)
10. Air pollutants

These factors require treatment in their own right and some may require admission to hospital. A high degree of suspicion is required to detect some relatively common disorders in the presence of COPD such as heart failure, pulmonary embolism and pneumothorax.

F. Initiate Pharmacotherapy for Acute Exacerbation

Objective

To initiate medication to improve respiratory function.

Annotation

Initiate or adjust short-acting inhaled beta2-agonists (SAIBA) and inhaled anticholinergic metered dose inhalers with spacer to maximum levels as appropriate.

Table. Medication for Acute Exacerbation

Medication	MDI Dose	Nebulizer Dose	Instructions
Short Acting Beta2-Agonists			
Albuterol	3-4 puffs q½-2 h	2.5 mg q½-2 h	Deliver medication

Metaproterenol	3-4 puffs q½-2 h	10-15 mg q½-2 h	with nebulizer if unable to use MDI with spacer (1)
Terbutaline	3-4 puffs q½-2 h	N/A	
Anticholinergics			
Ipratropium Bromide	3-6 puffs q2-4h	500 micrograms q2-4h	
Systemic Steroids	Oral		
Prednisone	40-60 mg q day		Taper off or change to qod within 1 to 2 weeks
Prednisilone	30-50 mg q day		
Theophylline	If on theophylline check level		Aim for levels of 5 to 12 micrograms/ml

1. Assess use of metered dose inhaler (MDI and spacer). Frequency and dose can be titrated as the patient's condition allows. Patient can be discharged on minimum dose or less.

Evidence

Short-Acting Inhaled Beta2-Agonists

Metaproterenol 1.95 mg (3 puffs) produced 18 percent increase in FEV_1: Level of Evidence: B; Strength of Recommendation: I (Karpel et al., 1990).

Albuterol 400 micrograms (4 puffs) over 60 min produced 22 percent increase in FEV_1: Level of Evidence: B; Strength of Recommendation: I (Lloberes et al., 1988).

Anticholinergics

Similar increase in FEV_1 following ipratropium or metaproterenol by MDI in ED and clinic patients: Level of Evidence: B; Strength of Recommendation: I (Karpel et al., 1990).

Similar increase in FEV_1 following ipratropium or metaproterenol by NEB in ED patients: Level of Evidence: B; Strength of Recommendation: I (Rebuck et al., 1987).

Combination Therapy

Combined agents produced similar increase in FEV_1 compared to fenoterol or ipratropium alone by NEB in ED patients: Level of Evidence: B; Strength of Recommendation: IIb (Rebuck et al., 1987).

Addition of ipratropium MDI to standard multidrug therapy did not increase improvement in FEV_1 over 24 hours in hospitalized patients: Level of Evidence: B; Strength of Recommendation: I (Patrick et al., 1990).

Ipratropium MDI shortened ED stay but did not alter FEV_1 in patients who received isoetharine NEB: Level of Evidence: B; Strength of Recommendation: I (Shrestha et al., 1991).

Addition of ipratropium by NEB did not improve PFR compared with albuterol NEB alone in ED patients: Level of Evidence: B; Strength of Recommendation: I (O'Driscoll et al., 1989).

Delivery Method

Similar benefit from MDI or NEB metaproterenol on dyspnea or FEV_1 in ED patients: Level of Evidence: B; Strength of Recommendation: IIa (Turner et al., 1988).

Similar effect of albuterol MDI or NEB on FEV_1 and dyspnea in hospitalized patients: Level of Evidence: B; Strength of Recommendation: IIa (Berry et al., 1989).

Benefit from NEB > MDI metaproterenol on FVC in hospitalized patients: Level of Evidence: B; Strength of Recommendation: IIa (Maguire et al., 1991).

Benefit from low- or high-dose albuterol NEB on FEV_1 in ED patients: Level of Evidence: B; Strength of Recommendation: IIa (Emerman et al., 1997).

Indications for Systemic Corticosteroid Therapy

More serious illness. Inadequate response to bronchodilators. Previous response to steroids: Level of Evidence: C; Strength of Recommendation: IIa (ATS Consensus Statement, 1995).

Systemic corticosteroids are used empirically in COPD exacerbation. Level of Evidence: C; Strength of Recommendation: IIa (Siafakas, 1995).

Suggest use in mild/moderate COPD exacerbation: Level of Evidence: C; Strength of Recommendation: IIa (Hudson & Monti, 1990).

Prednisone

Methylprednisolone added to standard multidrug therapy: Level of Evidence: B; Strength of Recommendation: IIa (Albert, Martin, & Lewis, 1980).

Early administration of methylprednisolone did not improve FEV_1 or reduce hospitalization in ED patients: Level of Evidence: B; Strength of Recommendation: IIa (Emerman et al., 1989).

IV and oral steroids reduced relapse rate in ED patients with COPD exacerbation and a history of relapses: Level of Evidence: B; Strength of Recommendation: IIa (Murata et al., 1990).

Oral prednisone improved FEV_1, and reduced treatment failure in veteran outpatients: Level of Evidence: B; Strength of Recommendation: IIa (Thompson et al., 1996).

Theophylline

Aminophylline did not add any observable benefit when added to standard multidrug therapy in hospitalized patients: Level of Evidence: B; Strength of Recommendation: IIa (Rice, 1987).

Aminophylline did not add any measurable or symptomatic benefit with a trend to decreasing admission rate in ED patients. Level of Evidence: B; Strength of Recommendation: IIa (Wrenn, 1991).

G. Is Patient's Condition Improved and Patient is Able to Go Home?

Objective

To identify patients who can go home.

Annotation

The following should be considered in evaluating the possibility of discharge:

1. Patient clinical condition has improved
2. Patient has adequate support system at home
3. Patient is able to continue necessary therapy at home (e.g., oxygen supply)

H. Has Patient's Condition Improved in 1 to 3 Days?

Objective

Identify improvement in COPD exacerbation.

Annotation

Evidence of improvement of COPD exacerbation includes:

1. Decrease in cough, sputum production or dyspnea

2. Decrease in respiratory rate
3. Decrease in heart rate
4. Increase in function and endurance

I. Slowly Taper Intensity of Medication(s) to Baseline Maintenance Regimen

Objective

Initiate appropriate reduction in medications in order to return to maintenance levels.

Annotation

1. Once the patient is stabilized, with improvement in the level of function, reduce intensity of the bronchodilator regimen down to the usual level of treatment over the course of a few days.
2. Tapering of corticosteroids depends on the prior history of use and tapering, but often is done over one to two weeks. This can be done in consultation with the primary care provider.
3. The provider should see the patient soon to ensure that the course of action is appropriate and for consideration of any further therapy such as smoking cessation, or changes in pharmacotherapy in view of the recent exacerbation.

Algorithm A2

Outpatient Management of COPD: Pharmacotherapy (Module A2)

A. Patient with COPD Requiring Pharmacotherapy

This algorithm outlines the criteria for the medication treatment of COPD. The aim of therapy is to use those medications needed to maintain control and improve function and quality of life with the least risk for adverse effects. The medication plan for COPD is summarized above in the table titled "Medication for Acute Exacerbation."

Table. Step Care In Chronic Obstructive Pulmonary Disease

Step	Symptoms and FEV_1	Therapy
1	Asymptomatic AND FEV_1 > 50 percent of predicted (1)	Smoking cessation, vaccination, employ education. No medication indicated.
2a	Symptoms less than daily AND $FEV_1 \geq$ 50 percent of predicted (2)	Smoking cessation, vaccination, employ education. Inhaled short-acting beta2-agonist (2 puffs PRN up to 12 puffs/day)
2b	Asymptomatic AND	Smoking cessation, vaccination,

	FEV_1 < 50 percent of predicted	employ education. Inhaled anticholinergic (2 puffs q.i.d) Consider use of inhaler containing a short acting beta2-agonist and an anticholinergic.
2c	Symptoms less than daily AND FEV_1 < 50 percent of predicted OR Daily symptoms	Smoking cessation, vaccination, employ education. Inhaled anticholinergic (2 puffs q.i.d) Short-acting beta2 agonist (2 puffs PRN up to 12 puffs/day) Consider use of inhaler containing a short acting beta2-agonist and an anticholinergic.
3	Symptoms not controlled (2)	Increase dose of both: Inhaled anticholinergic (2 to 6 puffs q.i.d) and inhaled short-acting beta2-agonist (2 -4 puffs PRN up to 12 puffs/day)
4	Symptoms not controlled(2)	Consider adding long-acting inhaled beta2-agonist. (3)
5	Symptoms not controlled (2)	Consider adding theophylline trial (slow release theophylline adjusted to level of 5 to 12 micrograms/ml) (4)
6	Symptoms not controlled (2)	Consider adding corticosteroid trial (prednisone 40 to 60 mg po qd or high dose inhaled steroids (5). Consider specialist consultation.
7	Symptoms not controlled (2)	Refer to specialist promptly.

1. Spirometry is essential to confirm the presence of airflow obstruction (low FEV_1 and FEV_1/VC ratio). Base therapy on symptoms, but consider alternate diagnoses (heart disease, pulmonary emboli, etc.) if out of proportion to spirometry.

2. Use the lowest level of therapy that satisfactorily relieves symptoms and maximizes activity level. Assure compliance and proper use of medications before escalating therapy.
3. Inhaled long acting beta2-agonists should not be used as rescue therapy. Short-acting inhaled beta2-agonist (less than 12 puffs/day) may continue to be used PRN. Nighttime symptoms are frequently better controlled with long-acting inhaled beta2-agonist. Oral beta2-agonists are associated with a higher rate of side effects, and should be reserved for patients who cannot take inhaled beta2-agonist medications.
4. Theophylline should be used with caution because of potential for severe side effects. Nighttime respiratory symptoms are frequently controlled but theophylline may lead to insomnia. Theophylline should be discontinued if a symptomatic or objective benefit is not evident within several weeks.
5. A corticosteroid trial of prednisone (40 to 60 mg/day) 10 to 14 days, or high dose inhaled steroids (equivalent to 880 micrograms or more of fluticasone or 800 micrograms or more of budesonide) of 14 to 21 days can help identify patients who may benefit from long term steroid use. Responders to oral steroids should transition to the lowest effective dose of inhaled steroids, or to the lowest effective dose of a combination of inhaled and oral steroids, if possible, to avoid the long term complications of systemic corticosteroids. If oral steroids are used other than for an acute exacerbation, obtain spirometry prior to and after trial to confirm an objective response.

B. Are Symptoms Occurring Less frequently than Daily AND FEV_1 is $\geq$ 50% of predicted?

Objective

To identify patients with COPD who may benefit from therapy.

Annotation

1. Typical daily symptoms of COPD include exertional dyspnea, wheezing, or cough. Chest tightness is common, but should be further evaluated to exclude co-existing heart disease. These symptoms may occur daily or less than daily, thus resulting in different medication recommendations.
2. Routine use of ipratropium does not slow the rate of decline in pulmonary function in patients with mild COPD. Patients with symptoms less often than daily may be medicated as needed.
3. A trial of inhaled anticholinergic therapy is recommended in apparently asymptomatic patients with an FEV_1 of less than 50 percent of predicted, since this degree of obstruction is usually associated with dyspnea. A lack of symptoms may result from the patient avoiding activities and adapting to his/her disability, or from the assumption that dyspnea is part of the natural aging process.
4. Asymptomatic patients with an FEV_1 less than 50 percent predicted may benefit from regular inhaled anticholinergic therapy without a short acting inhaled beta2-agonist (SAIBA). Symptomatic patients in this category should be prescribed both a chronic anticholinergic

inhaler or SAIBA as well as a beta2-agonist for p.r.n use, especially prior to exertion.

Evidence

Consensus recommendations on initiation of pharmacotherapy: Level of Evidence: C; Strength of Recommendation: IIa (ATS, 1995; Siafakas, 1995; BTS, 1997).

Ipratropium 36 micrograms tid for 5 years did not affect the rate of decline in FEV_1: Level of Evidence: A; Strength of Recommendation: I (The Lung Health Study, Anthonisen, 1994).

C. Short Acting Inhaled Beta2-Agonists

Objective

To initiate or adjust appropriate p.r.n therapy with SAIBA.

Annotation

1. Short acting beta2-agonists are available in MDI, dry powder inhalers, nebulizer and oral forms. They can improve function and quality of life.
2. Short-acting selective inhaled beta2-agonists such as albuterol are preferred for p.r.n use because of demonstrated efficacy, rapid action, and selective action on airways. The short-acting adrenergic agents have similar efficacy, though inhaled beta2 selective agents should be favored for lower side effect profiles.
3. SAIBA should be prescribed for p.r.n use in most symptomatic patients with COPD. The usual maximum dose in stable patients is 12 puffs per day for short-acting agents such as albuterol, metaproterenol or terbutaline. Patients who have not responded to greater than maximum doses such as 12 to 20 puffs over three to four hours during an acute exacerbation of COPD should seek medical attention.
4. Symptoms may improve without substantial improvement in FEV_1, indicating that continuation of therapy does not depend on routine assessment with spirometry. For example, SAIBA and ipratropium can improve exercise performance without necessarily improving FEV_1.
5. SAIBA, but not ipratropium, may increase the alveolar-arterial oxygen difference, and this may be a reason to decrease the dose of beta2-agonist while titrating a patient's medication.

Evidence

Metaproterenol inhalation (5 puffs) led to an improvement in the 12-minute walk that was not present with placebo. Spirometry was not improved: Level of Evidence: C; Strength of Recommendation: I (Berger, 1988).

Terbutaline (2 puffs = 500 micrograms) decreased breathlessness: Level of Evidence: B; Strength of Recommendation: IIa (Pino-Garcia, 1996).

Albuterol (270 micrograms) decreased breathlessness with exercise: Level of Evidence: B; Strength of Recommendation: I (Belman, 1996).

Pirbuterol and ipratropium produced similar increases in FEV_1. Pirbuterol increased the [A-a] O_2 difference: Level of Evidence: B; Strength of Recommendation: I (Ashutosh, 1995).

Significant dose-related improvement in spirometry with inhaled albuterol. One mg as a single dose offered most benefit versus side effects: Level of Evidence: B; Strength of Recommendation: I (Vathenen, 1988).

Average dose of albuterol inhalation for optimal improvement was 430 micrograms (range up to 800 micrograms) and for terbutaline was 1,160 micrograms (range up to 2.5 mg): Level of Evidence: B; Strength of Recommendation: I (Jaeschke, 1993).

D. Inhaled Anticholinergics

Objective

To initiate or adjust appropriate therapy with inhaled anticholinergics.

Annotation

1. Ipratropium bromide, the prototype anticholinergic bronchodilator, is available as a metered dose inhaler (MDI) or as a nebulizer solution.
2. Ipratropium bromide has similar, or according to some studies, greater efficacy than SAIBA. It has a slower onset of action, a longer duration of action, and minimal systemic absorption. It may cause fewer systemic side effects than beta2-agonists. For these reasons, it is preferred as a regularly scheduled inhaled bronchodilator.
3. In patients with COPD, ipratropium bromide at peak effect typically increases the FEV_1 by 0.15 to 0.35 L. At high doses, ipratropium bromide can improve exercise tolerance.
4. The starting dose of ipratropium should be at least two puffs tid. Use of typical recommended doses of ipratropium (two puffs q.i.d) produces less than maximal bronchodilation. Improvement in pulmonary function is maximal at 6 to 14 puffs as a single dose of ipratropium. If symptoms do not resolve with two to four puffs q.i.d, up to six and possibly eight puffs q.i.d may be needed. Improvement in level of function and in activities in daily living can be used to guide therapy. The risk of toxicity at higher doses appears to be relatively low compared to inhaled beta2-agonists.
5. The sequence of administration of ipratropium and SAIBA does not generally make any difference in the bronchodilator benefit.

Evidence

Baseline FEV_1 and FVC increased within 90 days after ipratropium initiation: Level of Evidence: B; Strength of Recommendation: IIa (Rennard, 1996).

Ipratropium 40 micrograms q.i.d (2 puffs) or metaproterenol 1.5 mg q.i.d by inhalation were equally efficacious and safe over a 90-day period: Level of Evidence: A; Strength of Recommendation: I (Tashkin, 1986).

No difference between 200 micrograms albuterol (2 puffs) and 40 micrograms ipratropium in magnitude, but duration was 1 hour longer with ipratropium on day 85: Level of Evidence: A; Strength of Recommendation: I (COMBIVENT Inhalation Aerosol Study Group, 1994).

Ipratropium produced more and longer bronchodilation than did albuterol: Level of Evidence: A; Strength of Recommendation: IIa (Braun, 1989).

The distance walked was greater with 7 days of albuterol (180 micrograms, 2 puffs) or ipratropium (36 micrograms) q.i.d (2 puffs); also dyspnea was less with albuterol: Level of Evidence: B; Strength of Recommendation: IIa (Blosser, 1995).

Of 80 responsive patients in a group of 100, 16 responded only to albuterol; 17 responded only to ipratropium; and 47 responded to both: Level of Evidence: C; Strength of Recommendation: IIa (Nisar, 1992).

Between 6 and 14 puffs of ipratropium (240 micrograms) produced maximum increase in pulmonary function: Level of Evidence: B; Strength of Recommendation: I (Ikeda, 1995).

160 micrograms of ipratropium (8-9 puffs) is needed to give maximum benefit in pulmonary function and to give any benefit at all with exercise: Ikeda 1996. Level of Evidence: B; Strength of Recommendation: I (Ikeda, 1996).

0.4 mg of nebulized ipratropium provided a maximum response in pulmonary function. Suggested this was equivalent to 160 micrograms (8-9 puffs) from MDI: Level of Evidence: B; Strength of Recommendation: IIa (Gross, 1989).

E. Combination Therapy with Inhaled Anticholinergics and Short Acting Beta2-Agonists

Objective

To initiate or adjust appropriate therapy with a combination of inhaled SAIBA.

Annotation

1. Patients with COPD whose symptoms are inadequately controlled with the recommended doses of either an inhaled short acting inhaled beta2-agonist or ipratropium should be treated with a combination of both inhaled agents. The combination at recommended doses provides added symptomatic benefit without incurring the risk of toxicity from using very high doses of single agents.
2. SAIBA may be added to ipratropium as regularly scheduled medications, typically two to four puffs q.i.d, as well as additional p.r.n

dosing, to a usual recommended maximum of 12 puffs per day. Demonstration of an acute improvement in FEV_1 is not necessary in order to obtain clinical benefit. The lack of an immediate bronchodilator response should not preclude a clinical trial of these medications.

3. As the dose of ipratropium or inhaled SAIBA increases, the added benefit becomes less from the other agent, but some patients will have an added benefit even with high doses of each. There is no way to predict, other than in a trial of therapy, which patients will have this combined effect.
4. A product that dispenses 90 micrograms albuterol and 18 micrograms ipratropium per puff from one metered dose inhaler is available commercially (Combivent™). This should not generally be used as a first line agent, but may provide enhanced compliance and resultant benefit in patients who require combination therapy. Patients taking a regularly scheduled combination inhaler should continue to use a SAIBA for breakthrough symptoms.

Evidence

80 micrograms ipratropium (4 puffs) plus 400 micrograms (4 puffs) albuterol was better than 40 micrograms or 80 micrograms ipratropium plus 200 micrograms albuterol in improving FEV_1: Level of Evidence: C; Strength of Recommendation: I (Ikeda, 1995).

There was no added benefit of doubling the ipratropium dose or adding 1,300 micrograms of inhaled metaproterenol. Two of 12 patients benefited from this combination: Level of Evidence: B; Strength of Recommendation: I (LeDoux, 1989).

40 micrograms ipratropium plus 200 micrograms inhaled albuterol yielded a greater increase in pulmonary function than did either 40 micrograms ipratropium or 200 micrograms albuterol: Level of Evidence: A; Strength of Recommendation: I (COMBIVENT Inhalation Aerosol Study Group, 1994).

120 micrograms of ipratropium or 800 micrograms of albuterol gives maximal bronchodilation in a single dose. Some patients may benefit from combination: Level of Evidence: B; Strength of Recommendation: IIa (Easton, 1986).

200 micrograms ipratropium added to 5 mg terbutaline or 500 micrograms terbutaline added to 200 micrograms ipratropium improved pulmonary function: Level of Evidence: C; Strength of Recommendation: IIa (Newnham, 1993).

F. Consider Adding Long-Acting Inhaled Beta2-Agonist

Objective

To initiate or adjust appropriate therapy with long acting inhaled beta2-agonists.

Annotation

1. The long acting inhaled beta2-agonist, salmeterol (2 puffs or 50 micrograms bid), is an effective bronchodilator in COPD patients, and has been approved for use in COPD.
2. Salmeterol produces a similar peak bronchodilator response to SAIBA, but the onset is delayed. The bronchodilator effect is prolonged compared to short-acting agents. This has the potential to produce more consistent control of symptoms than SAIBA in some patients.
3. Chronic use is not associated with significant tachyphylaxis, and may decrease the need for rescue use of SAIBA.
4. Strong evidence for symptomatic benefit of salmeterol over other regularly inhaled short acting bronchodilators in patients with COPD is not currently available. Thus, its place in the scheme of therapy is not well defined at this time. It may be considered for patients whose need for SAIBA exceeds 8 to 12 puffs daily.
5. The principle advantage of salmeterol is its long duration of action, which may be of benefit in treating nocturnal dyspnea. Additionally, enhanced compliance with a twice daily rather than q.i.d regimen may provide smoother symptomatic control.
6. Because the onset and duration of action are both prolonged compared to SAIBA, salmeterol should not be used for p.r.n, rescue use. Patients should be educated to continue to use SAIBA p.r.n.
7. Oral forms of beta2-agonists may be useful in patients who cannot use any inhaled form, although such cases are rare. The risk of systemic adverse reactions is increased significantly with oral beta2 adrenergic bronchodilators.
8. Inhaled salmeterol should be continued only in those patients who experience symptomatic benefit from its addition to their regimen.

Evidence

Four weeks of 50 micrograms bid (or 2 puffs) salmeterol led to an increase in FEV_1: Level of Evidence: B; Strength of Recommendation: I (Grove, 1996).

16 weeks of treatment with 50 micrograms bid salmeterol added to existing regimen improved FEV_1 and symptoms: Level of Evidence: A; Strength of Recommendation: I (Boyd, 1997).

16 weeks of 50 micrograms bid (but not 100 micrograms bid) salmeterol improved health related quality of life: Level of Evidence: A; Strength of Recommendation: I (Jones, 1997).

Salmeterol acute dose response curve plateaus at 50 micrograms: Level of Evidence: B; Strength of Recommendation: I (Cazzola, 1995).

4 weeks of 50 micrograms bid salmeterol improved peak flow and symptoms: Level of Evidence: A; Strength of Recommendation: I (Ulrik, 1995).

Combination of salmeterol (50 micrograms) and ipratropium was no different than either alone for peak effect; duration was similar to that for salmeterol: Level of Evidence: B; Strength of Recommendation: IIb (Matera, 1996).

Single-dose 50 micrograms salmeterol caused more prolonged acute bronchodilation than 200 but not 400 micrograms oxitropium inhaler: Level of Evidence: B; Strength of Recommendation: IIa (Cazzola, 1998).

G. Consider Theophylline Trial

Objective

To initiate or adjust appropriate therapy with oral theophylline.

Annotation

1. Theophylline can be added to improve pulmonary function, symptoms, or activities in patients with COPD who do not achieve adequate symptom control with inhaled bronchodilators.
2. Many theophylline preparations are available, but sustained release formulations may provide longer control and better benefit for nocturnal dyspnea.
3. Theophylline has a narrow therapeutic index, with the potential for dose related adverse reactions that include insomnia, anxiety, nausea, vomiting, tremor, arrhythmias, delirium, seizures, and death.
4. Typical starting doses are 400 to 600 mg daily, but blood levels should be measured carefully at the start of therapy. The therapeutic target for most patients should be a blood level of 10 micrograms/ml (range 5-12 micrograms/ml). In some cases, if benefit has been demonstrated and with careful monitoring, a blood level of 15 micrograms/ml of theophylline can be a therapeutic target. However, with an increase in concentrations over 12 micrograms/ml, the risk to benefit ratio increases, especially in older patients. After initial stability, repeat levels should be obtained when symptoms change, acute illness develops, potentially interacting drugs are added, non-compliance is suspected, dose adjustments are made, or symptoms suggestive of toxicity develop.
5. Drug interactions with theophylline are common, and may either increase or decrease theophylline metabolism. All changes in medical regimens should be evaluated for potential impact on theophylline levels.
6. Theophylline should be continued only in patients who demonstrate a symptomatic benefit, such as improved dyspnea or exercise tolerance. The improvement in function from theophylline may not be evident in pulmonary function testing. However, therapy should be discontinued in patients who demonstrate no subjective or objective improvement after several weeks of theophylline therapy.

Evidence

<u>Mechanism of Benefit</u>

Theophylline is usually a bronchodilator: Level of Evidence: A; Strength of Recommendation: I (Fragoso, 1993).

Mucociliary clearance improved in some patients: Level of Evidence: C; Strength of Recommendation: IIa (Fragoso, 1993).

Some patients have an improvement in respiratory muscle performance: Level of Evidence: B; Strength of Recommendation: IIa (Fragoso, 1993).

Generally consistent improvement in function of the right heart: Level of Evidence: C; Strength of Recommendation: IIa (Fragoso, 1993).

Theophylline may increase respiratory drive: Level of Evidence: B; Strength of Recommendation: IIa.

Theophylline Therapy

Two months of theophylline at 14.8 micrograms/ml led to less dyspnea, an increase in PaO_2, a decrease in $PaCO_2$, and an increase in VC and FEV_1: Level of Evidence: A; Strength of Recommendation: IIa (Murciano, 1989).

Pulmonary function and exercise performance were improved on 9.5 mg/L of theophylline: Level of Evidence: B; Strength of Recommendation: IIa (Newman et al., 1984).

17 mg/L improved pulmonary function and symptoms: Level of Evidence: B; Strength of Recommendation: IIa (McKay, 1993).

Withdrawal of theophylline (11 mg/L) led to a decline in pulmonary function, an increase in symptoms, and less distance in the 6-minute walk test: Level of Evidence: A; Strength of Recommendation: IIa (Kirsten et al., 1993).

Theophylline at 12.2 mg/L improved FVC_1, MVV, and exercise: Level of Evidence: B; Strength of Recommendation: IIa (Fink, 1994).

Higher awake PaO_2, lower awake $PaCO_2$, higher sleep SaO_2, improved FEV_1, and lower trapped gas volume were seen with a theophylline level of 11.8 mg/L: Level of Evidence: B; Strength of Recommendation: IIa (Mulloy, 1993).

Theophylline (14.2 mg/L) improved FEV_1; SaO_2 increased during non-rapid eye movement (NREM) sleep. There were fewer arousals; sleep architecture was unaffected: Level of Evidence: B; Strength of Recommendation: IIa (Berry, 1991).

Twice-a-day theophylline (15 micrograms/ml) improved FEV_1 more than once a day (11 micrograms/ml). No effect on arterial saturation or sleep architecture: Level of Evidence: B; Strength of Recommendation: IIa (Martin, 1992).

Theophylline (9.2 micrograms/ml) improved pulmonary function, reduced nocturnal wheezing, and improved nocturnal saturation. Sleep quality unaffected: Level of Evidence: B; Strength of Recommendation: IIa (Man, 1996).

Theophylline Combination Therapy

Theophylline (12.5 mg/L) significantly improved FEV_1 and PEF (daily) to a small degree, even after the inhalation of salbutamol and ipratropium: Level of Evidence: B; Strength of Recommendation: IIa (Nishimura, 1993).

In combination with 400 micrograms salbutamol q.i.d and 80 micrograms (or 4 puffs) ipratropium q.i.d, theophylline (15 mg/L) had a small additive effect on FEV_1 and PEF: Level of Evidence: B; Strength of Recommendation: IIa (Thomas, 1992).

Theophylline (12.9 mg/L) and salbutamol improved pulmonary function; the combination was better than either alone: Level of Evidence: B; Strength of Recommendation: IIa (Thomas, 1992).

Combination theophylline (12 to 18mg/L), albuterol, and ipratropium improved pulmonary function more than did theophylline and albuterol or ipratropium alone: Level of Evidence: A; Strength of Recommendation: IIa (Karpel, 1994).

H. Consider Corticosteroid Trial

Objective

To initiate or adjust appropriate therapy with corticosteroids in patients with COPD.

Annotation

1. Unlike the high response rate seen in asthma, in patients with COPD a response to chronic oral corticosteroid use is beneficial in less than about 20 to 25 percent. The benefit from inhaled steroids is not precisely defined.
2. Patients on maximal bronchodilator therapy who have not had a satisfactory response may be considered candidates for a corticosteroid trial. An objective measure of improvement should be sought in all patients undergoing a steroid trial. A response may be defined as an improvement in symptoms and an increase in FEV_1 of $\geq$ 20 percent from baseline. An objective measurement of the steroid effects can only be obtained in patients who are otherwise stable.
3. A typical trial of oral prednisone is 40 to 60 mg/day for 10 to 14 days. There is less published experience with high-dose inhaled steroids, but in some patients this may be a reasonable alternative. The appropriate dose of inhaled steroids has not been determined, but a trial for 14 to 21 days of the equivalent of beclomethasone 1500 micrograms/day (30 puffs) or fluticasone 880 micrograms/day has been suggested.
4. Patients who show no objective response to a steroid trial should have their steroids promptly discontinued. Patients who have a response should be tapered to the lowest possible dose. Supplementation or substitution with a high-dose inhaled steroid may allow further reduction or discontinuation of the oral steroid.

5. Adverse effects of oral corticosteroids are numerous and include: hypertension, hyperglycemia, weight gain, immunosuppression, skin thinning, personality, purpura, mental status changes, depression, glaucoma, cataracts, and adrenal suppression. Patients requiring long-term steroids should be evaluated for risk of osteoporosis and preventive measures instituted, such as calcium and vitamin D supplements, weight-bearing exercise and hormone replacement therapy if appropriate. The risks of long-term treatment should be discussed with the patient.
6. The role of chronic inhaled corticosteroids in COPD remains under investigation. Preliminary work suggests that chronic inhaled steroid use may slow the rapid decline in FEV_1 typically seen in patients with COPD. Response to an oral steroid trial, as well as a brisk bronchodilator response may help identify patients who will respond better to inhaled steroids.
7. The use of MDI spacers and rinsing of the mouth after drug use is recommended to help improve drug delivery to the lung and avoid local complications, such as hoarseness or oral candidiasis.

Evidence

Oral steroid meta-analysis: 10 percent of patients with COPD using oral steroids (30 to 80 mg/day or equivalent prednisone) had a 20 percent improvement in FEV_1: Level of Evidence: A; Strength of Recommendation: I (Callahan, 1991).

Alternate-day oral steroids (64 mg) as effective as daily oral steroids (8 mg q.i.d): Level of Evidence: A; Strength of Recommendation: I (Blair, 1984).

Equal or more than 7.5 mg/day oral prednisolone slows decline of FEV_1 and improves survival in severe COPD: Level of Evidence: C; Strength of Recommendation: IIa (Postma, 1985).

7.5 mg/day oral prednisolone or more decreases decline in FEV_1 in moderately severe COPD: Level of Evidence: C; Strength of Recommendation: IIa (Postma, 1988).

40 mg/day of prednisolone added to inhaled beclomethasone of 1,500 and 3,000 micrograms/day did not further improve pulmonary function Level of Evidence: A; Strength of Recommendation: IIa (Weir, 1993).

It can take more than 2 weeks to reach maximum benefit from oral (40 mg prednisolone) or inhaled (1,500 micrograms beclomethasone) steroids: Level of Evidence: A; Strength of Recommendation: I (Weir, 1990).

Emphysema and nonemphysema COPD respond similarly to oral prednisolone (40 mg/day) and inhaled beclomethasone (1,500 micrograms/day): Level of Evidence: B; Strength of Recommendation: I (Weir, 1991).

20 of 100 subjects responded to 30 mg prednisolone for 2 weeks, 17 of whom responded to ipratropium or albuterol and 3 of whom were nonresponders: Level of Evidence: C; Strength of Recommendation: IIa (Nisar, 1992).

Inhaled beclomethasone (1,500 micrograms/day) produced 2/3 the response of oral prednisolone. Response to oral correlated with response to inhaled steroid: Level of Evidence: A; Strength of Recommendation: I (Weir, 1990).

Response to high-doses inhaled beclomethasone (1,500 micrograms/day) predicts which patients will respond to oral prednisolone (30 mg/day): Level of Evidence: C; Strength of Recommendation: IIa (Wardman, 1988).

Addition of oral prednisolone (30 mg/day) produces further improvement in responders to inhaled beclomethasone (1,500 micrograms/day): Level of Evidence: C; Strength of Recommendation: IIa (Wardman, 1988).

Meta-analysis: More than 800 micrograms of inhaled beclomethasone or budesonide was required for improvement in pulmonary function or symptoms: Level of Evidence: B; Strength of Recommendation: IIa (van Schayck, 1995).

Two years of 800 micrograms/day of budesonide plus either albuterol or ipratropium reduced the decline in FEV_1 and improved symptoms: Level of Evidence: C; Strength of Recommendation: IIa (Dompeling, 1993).

800 micrograms/day of budesonide for 12 weeks decreased cough but did not improve any other measure or symptom: Level of Evidence: B; Strength of Recommendation: IIa (Engel, 1989).

Two years of budesonide at 1,600 micrograms/day improved symptoms, and there were fewer dropouts for pulmonary reasons compared to placebo: Level of Evidence: A; Strength of Recommendation: IIa (Renkema, 1996).

Six weeks of 800 micrograms/day of budesonide improved 5 of 8 beta2-agonist acute responders and 1 of 22 nonresponders to beta2-agonist: Level of Evidence: B; Strength of Recommendation: IIa (Weiner, 1995).

Inhaled fluticasone (500 micrograms bid) for 6 months improved FEV_1, peak flow, 6 minute walk, symptoms and severity of exacerbations: Level of Evidence: A; Strength of Recommendation: IIa (Paggiaro, 1998).

I. Review Precautions and Recommendations for Medications?

Objective

To apply precautions and educate patients about the use of medications.

Annotation

Method of administering aerosols

1. Metered-Dose Inhalers (MDI)
    a. Inhaled bronchodilators are preferred to oral medications to reduce the risk of systemic adverse effects.
    b. Ensure proper education and technique in the use of MDIs.
    c. Use spacers as required to enhance drug delivery.
    d. Emphasize the maximum doses of bronchodilators to avoid overuse.
    e. Educate the patient to use bronchodilators before exercise.
    f. Compliance declines when inhaler regimens become complicated.
    g. Consider other drug delivery systems (such as dry powder inhalers) if patient cannot use MDI with spacer.
2. Small Volume Nebulizer
    a. There is little evidence that nebulizer delivery offers improvement in control over adequate MDI delivery for management of the stable COPD patient.
    b. Situations where a nebulizer is preferable include difficulty in managing a MDI (with spacer) due to impaired hand strength or dexterity, visual impairment, cognitive problems, or severe dyspnea.
3. Precautions when using beta2-agonists
    a. Inhaled beta2-agonists may cause tremor, increased heart rate, insomnia, restlessness, hypokalemia, or a paradoxical reduction in arterial oxygenation.
    b. Avoid overuse. Check number of metered dose inhalers (MDIs) used per month against number of puffs per MDI (200 to 300+, depending on brand).
    c. Instruct patients on maximum number of puffs per day (usually 8 to 12) and on number allowed during an exacerbation (e.g., 12 to 24 over 3 to 4 hours) before additional intervention is required.
    d. If a long-acting agent is used for maintenance therapy, educate the patient that only SAIBA should be used for breakthrough symptoms.
    e. Home nebulizers with inhalant solutions providing large dosages are rarely needed.
4. Precautions when using ipratropium
    a. Inhaled ipratropium may cause dry mouth or increased heart rate, or exacerbate glaucoma, benign prostatic hypertrophy or other conditions potentially worsened by the drug's anti-cholinergic activity.
    b. Patients should generally use a spacer and should avoid spraying into eyes.
    c. Caution patients that onset of effect is relatively slow compared to SAIBA, and that additional doses should not be taken for acute symptom relief.
    d. In general, dose related systemic side effects of inhaled anticholinergics are less severe when using ipratropium than those produced by inhaled beta2-agonists.
5. Precautions when using theophylline
    a. Theophylline has dose related side effects that include insomnia, anxiety, nausea, vomiting, tremor, arrhythmias, delirium, seizures, and death.

b. Drug interactions with theophylline are common, and all changes in a patient's medical regimen should be reviewed for their potential impact on serum theophylline levels.
c. Initiate treatment with a low dose (e.g., 400 mg/day) and adjust after a few days.
d. Aim for a serum level of 5 to 12 micrograms/ml; adjust dosage and follow serum level when indicated.
e. Check the serum level of theophylline when symptoms change, acute illness develops, new drugs are added, or symptoms suggestive of toxicity develop.
f. Reduce dosage if drug clearance is likely to be impaired because of illness, liver malfunction, or concomitant drugs.
g. Instruct patients not to take additional theophylline preparations.
h. Theophylline should be taken at the same time each day with respect to meals.
i. Attempts to withdraw theophylline, even at lower plasma levels, should be done cautiously, since deterioration in pulmonary function and exercise performance may occur.

6. Precautions when using oral corticosteroids
    a. Adverse effects of oral corticosteroids include hypertension, hyperglycemia, weight gain, personality changes, depression, immunosuppression, glaucoma, cataracts, skin thinning, purpura, osteoporosis, osteonecrosis, and adrenal suppression. In general, side effects are more common with prolonged therapy.
    b. Reduce dosage to lowest effective daily dose or to alternate-day dosing as quickly as symptoms allow.
    c. Administer stress dose steroid therapy to patients with severe illness or injury who have received prolonged oral corticosteroid treatment. Adrenal insufficiency may extend for up to a year following the discontinuation of steroids.
    d. Prevent or treat osteoporosis with calcium, vitamin D, hormone replacement therapy or other therapies as appropriate for patients on prolonged oral corticosteroid therapy.
7. Precautions when using inhaled corticosteroids
    a. Adverse effects of inhaled corticosteroids include oral candidiasis, hoarseness, and possible adrenal suppression at high doses.
    b. Instruct patients to use a spacer and rinse the mouth after use to decrease the likelihood of local complications.
    c. Be aware that systemic effects of corticosteroids may occur in skin, bone, eyes, and other organs, especially with the use of high dose inhaled corticosteroids.
    d. Stress dose oral or intravenous corticosteroids may be necessary in some patients with severe illness or injury who have been treated with high dose inhaled corticosteroids.
    e. Seek objective evidence of the value of this therapy, because its use may decrease compliance with other aerosol usage.
    f. When introducing aerosol steroids in a patient taking an oral steroid, wean slowly off the oral drug.

Evidence

Precautions when using pharmacotherapy: Level of Evidence: C; Strength of Recommendation: IIa (ATS, 1995).

MDI technique: Level of Evidence: C; Strength of Recommendation: IIa (Newman, 1984).

52 percent used an MDI once or less daily rather than the required three times daily: Level of Evidence: C; Strength of Recommendation: I (Rand, 1995).

Adherence with intermittent positive pressure breathing (IPPB) or nebulizers was 50.6 percent: Level of Evidence: C; Strength of Recommendation: I (Turner, 1995).

Maximum bronchodilation was similar between nebulizer and MDI beta2-agonist. Nebulizer dose of twice MDI dose to produce same effect: Level of Evidence: B; Strength of Recommendation: I (Mestitz, Copland & McDonald, 1989).

Dose of nebulized albuterol producing the same bronchodilation was about 10 times higher than with MDI: Level of Evidence: B; Strength of Recommendation: I (Jenkins, 1987).

No difference in outcome between nebulizer and MDI. Nebulized metaproterenol dose was about seven times higher than with the MDI: Level of Evidence: B; Strength of Recommendation: I (Turner, 1988).

It takes about 12.5 times as much nebulized albuterol to achieve the same increase in FEV_1 as with an MDI: Level of Evidence: B; Strength of Recommendation: I (Harrison, 1983).

Algorithm A3

Outpatient Management of COPD: Long-term Oxygen Therapy (Module A3)

A. Patient with COPD on Maximal Medical Therapy and Stable for 30 Days

Objective

In COPD, patients with hypoxemia and cor pulmonale, long-term oxygen therapy (LTOT) may increase the life span by six to seven years. Mortality is reduced in patients with chronic hypoxemia when oxygen is administered for more than 12 hours daily and greater survival benefits have been shown with continuous oxygen administration.

Annotation

Patient should be on maximal medical therapy and stable for 30 days before decisions about LTOT are made. Short-term oxygen may be instituted in the

interim. In addition to treating acute exacerbations, therapy to correct anemia and congestive heart failure should be instituted. Intensify smoking cessation efforts, since smoking poses a safety hazard for patients on LTOT. The benefits of long-term oxygen therapy may not be realized in patients who continue to smoke and have high levels of carboxyhemoglobin.

Evidence

LTOT prolongs life in hypoxemic patients, with greater benefit with 24-hr/day than 12-hr/day therapy: Level of Evidence: A, C; Strength of Recommendation: I (Timms, 1981; Levi-Valensi, 1986).

B. Are There Signs of Tissue Hypoxia?

Objective

To identify patient with signs of tissue hypoxia who may benefit from LTOT.

Annotation

Occasionally severe dyspnea with exercise is the result of arterial oxygen desaturation. Evaluation of saturation during exercise should be performed in COPD patients with such dyspnea.

Signs of tissue hypoxia include:

1. Hematocrit (Hct) greater or equal 55
2. "p" pulmonale on electrocardiogram (ECG) or other evidence of pulmonary hypertension
3. Impaired mental status
4. Cor pulmonale

C. Is $PaO_2 \leq 55$ mm Hg?

Objective

To identify hypoxemia.

Annotation

Based on a randomized controlled trial, long-term oxygen therapy of COPD patients with a $PaO_2 \leq 55$, or a $PaO_2 \leq 60$ with signs of tissue hypoxia, is associated with improved survival. Although pulse oximetry can be used to exclude hypoxemia, measurement of resting PaO_2 after 30 minutes of breathing room air is the clinical standard for initiating LTOT. Oximetry may be used to adjust oxygen flow settings over time.

Evidence

Pulse oximetry is less accurate than arterial blood gases to determine oxygenation, especially during exercise: Level of Evidence: C; Strength of

Recommendation: I (Carone, 1997; Carlin, 1994; McGovern, 1996; ATS, 1995; Pierson, 1990).

D. Institute Long-Term, 24-Hour Oxygen Therapy

Objective

To define the goals of oxygen therapy.

Annotation

The precise PaO_2 level to improve quality of life or increase survival has not been well defined. Arterial oxygen saturations of 90 to 92 percent or PaO_2 of 60 to 65 mmHg are usual acceptable targets because of the shape of the oxygen hemoglobin saturation curve. Ambulatory patients should be provided ambulatory and stationary oxygen equipment to reach the target of use 24 hours a day to correct PaO_2 greater or equal 60 or SaO_2 greater or equal 90 percent. Immobile patients may only require a stationary system with a portable system for use during transport. In most cases, changes in flow rate are not indicated for sleep and exercise. Some authorities recommend increasing flow rates by one liter per minute to treat possible desaturation during sleep, but evidence for this approach is not strong. If there are signs of cor pulmonale despite adequate daytime oxygenation, the patient may be monitored with oximetry during sleep to determine the best sleep setting. Some patients may be candidates for oxygen-conserving devices (e.g., reservoir cannulae, demand oxygen delivery device, transtracheal oxygen) to improve mobility and portability of oxygen therapy.

Evidence

Oxygen-conserving devices may reduce costs and increase patient mobility: Level of Evidence: C; Strength of Recommendation: IIa. (ATS, 1995; Petty, 1994).

E. Order Overnight Oximetry and/or Exercise Oximetry

Objective

To identify patients with PaO_2 desaturation who may benefit from LTOT.

Annotation

It is unusual that patients with COPD and a PaO_2 of 70 at rest to desaturate low enough to require oxygen. During exercise, noninvasive pulse oximetry may be inaccurate, particularly in patients with poor peripheral perfusion. Verification of oximetry accuracy can be accomplished by obtaining ABG before and after exercise. The level of exercise tested should be appropriate to the patient's normal or anticipated level of activity.

In COPD patients who have $PaO_2 \geq 60$ mmHg during wakefulness, signs of tissue hypoxia occur more often and survival is reduced when sleep

desaturation is present (more than five minutes during the night). However, studies documenting improved outcome with oxygen supplementation during sleep have yet to be conducted. One night of overnight oximetry is sufficient to determine the present of arterial oxygen desaturation during sleep. Such desaturation can occur as the patient's COPD evolves with time and the overnight oximetry may need to be repeated at regular intervals (such as six months to yearly) in patients who have or develop an indication.

Evidence

Nocturnal oxygen therapy in patients who have daytime PaO_2 60 mmHg with nocturnal desaturation of less than 90%: Level of Evidence: C; Strength of Recommendation: IIa (Fletcher, 1989, 1992a, 1992b).

Exercise desaturation does not predict nocturnal desaturation: Level of Evidence: C; Strength of Recommendation: IIa (Baldwin, 1995).

A diffusing capacity greater than 55% of predicted was 100% specific in excluding exercise desaturation compared with 82% specificity for FEV_1 > 55% of predicted: Level of Evidence: C; Strength of Recommendation: IIa (Owens, 1984).

One overnight oximetry is sufficient to diagnose nocturnal desaturation in stable COPD patients: Level of Evidence: C; Strength of Recommendation: IIa (Vos, 1995).

F. Arrange for Long-Term Oxygen Therapy During Sleep and/or Exercise

Objective

To discuss the benefits of oxygen therapy

Annotation

Studies showing the long-term benefit of oxygen solely for exercise or sleep desaturation have yet to be conducted. Short-term studies have shown more immediate benefits in reduction in dyspnea, improvement in exercise performance, and prevention of transient increases in pulmonary artery pressure and pulmonary vascular resistance. Oxygen should be administered to increase SaO_2 to greater than 90 percent. To maximize mobility, liquid or light tanks such as those made from aluminum are preferable for use during exercise.

Evidence

Oxygen during exercise provides short-term physiologic benefits, reduces dyspnea, and improves exercise tolerance at submaximal workloads: Level of Evidence: C; Strength of Recommendation: IIa (McDonald, 1995; ATS, 1995; Light, 1989; Zack, 1985).

Lightweight portable ambulatory equipment should be used for patients who are able and willing to be active: Level of Evidence: C; Strength of Recommendation: IIa (Petty, 1994).

G. Continue Medical Care and Follow-up

Objective

To continue with appropriate follow up of oxygen therapy.

Annotation

Patients started on oxygen therapy at the time of an exacerbation require reevaluation within one to three months when stable. For patients started when stable on maximal medical therapy, LTOT most likely represents a lifetime commitment. Reevaluation every 12 months is appropriate to assess for continued need and adequacy of flow rate. Results of O_2 saturation greater than 90 percent should not be used as a sole rationale for discontinuing therapy.

Evidence

Increased PaO_2 after 6 months LTOT may be due to reparative effect of LTOT: Level of Evidence: C; Strength of Recommendation: IIa (Summary of the 3d Consensus Conference, 1990; O'Donohue, 1991).

H. If ABGs Are Available, Is $PaCO_2$ 45 mmHg?

Objective

Identify COPD patients with hypercarbia and its relationship to hypoxia.

Annotation

Hypercapnia during the day predicts a high prevalence of sleep desaturation even in patients who have PaO_2 60 mm Hg during wakefulness. Noninvasive ventilation for treatment of nocturnal hypoventilation for chronic home use has been investigated but unproven and is not endorsed for general use.

Evidence

Hypercapnia ($PaCO_2$ greater than 45) during the day predicts a high prevalence of nocturnal arterial oxygen desaturation: Level of Evidence: C; Strength of Recommendation: I (Littner, 1980; Fletcher, 1991; Douglas, 1990; Mulloy, 1995; Vos, 1995).

NPPV + nocturnal O_2 improved ABGs, sleep efficiency, quality of life, respiratory muscle function: Level of Evidence: B; Strength of Recommendation: IIa (Meecham Jones, 1995; Gigliotti, 1994; Ambrosino, 1992).

NPPV + nocturnal O_2 did not improve ABGs, sleep efficiency, quality of life, respiratory muscle function: Level of Evidence: B; Strength of Recommendation: IIa (Lin, 1996; Strumpf, 1991; Shapiro, 1992).

Algorithm A4

Outpatient Management of COPD: Preoperative Evaluation and Management (Module A4)

A. Does Condition Require Emergency Surgery?

Objective

To refer patients who need emergency surgery

Annotation

In-hospital respiratory specialist or intensivist should be notified for perioperative care, but emergency surgeries, including repair of femoral neck and hip fractures, should not be held up pending consultation.

B. Inform Physician in Charge of Postoperative Care of COPD Condition. Stress Need for IV Corticosteroids if Patient is on Systemic Steroids

Objective

To ensure proper care for the patient at risk.

Annotation

Determine whom to call when emergency surgery is performed. An in-house respiratory specialist should be notified for perioperative care. If the patient is on systemic steroids, switch to IV steroids using hydrocortisone 300 mg/day or an equivalent.

C. Is This a Minor Surgery Requiring Local Anesthesia?

Objective

To determine need for patients undergoing local anesthesia for minor surgery.

Annotation

Administration of local anesthesia presents a very low risk, even in the presence of severe COPD. In clinically stable patients with mild or moderate COPD, a phone inquiry about exacerbation might suffice. Pulmonary function test (PFT) is not required.

Evidence

Cataract surgery is very low risk even with COPD: Level of Evidence: C; Strength of Recommendation: IIa (Gozurn, 1992).

Ophthalmic procedures carry a low ($\leq$ 1 percent) mortality rate: Level of Evidence: C; Strength of Recommendation: IIa (ATS, 1995).

D. Obtain Pulmonary Function Tests, Arterial Blood Gases

Objective

To obtain spirometry values to guide the decision about preoperative care.

Annotation

There is no universal opinion on the value of pulmonary function testing preoperatively. A common opinion is that when a preoperative evaluation of a patient about to undergo elective CABG surgery suggests lung disease, simple spirometry can better characterize the nature of the patient's pulmonary problems and aid in the decision about appropriate preoperative medical therapy. One study showed that low FEV_1 predicted postoperative complications such as prolonged ICU stay, prolonged hospital stay, prolonged mechanical ventilation, and pneumonias, but this study involved only patients with severe COPD ($FEV_1 \leq 1.2$ L), with mixed surgical sites. On the other hand, other studies have shown that pulmonary function testing does not predict perioperative complications.

Evidence

Spirometry does not predict postoperative complications: Level of Evidence: B; Strength of Recommendation: IIb (Kroenke, 1993).

Spirometry cannot be performed reliably in the presence of abdominal pain: Level of Evidence: C; Strength of Recommendation: IIb (Hall, 1991b).

$FEV_1 < 0.75$ L raises the risk of prolonged ICU stay and $FEV_1/FVC < 0.5$ raises the risk of all postoperative pulmonary complications, such as pneumonia and prolonged hospital stay: Level of Evidence: B; Strength of Recommendation: IIb (Wong, 1995).

Spirometry can aid in the decision about appropriate perioperative care: Level of Evidence: C; Strength of Recommendation: IIb (Zibrak, 1990).

E. Obtain Chest X-Ray

Objective

To identify patients at risk for developing complications.

Annotation

Chest X-ray should be done preoperatively in patients with an established diagnosis of COPD who may require general anesthesia, since an abnormal chest X-ray is a predictor of perioperative complications in thoracic and major abdominal surgery. A preoperative chest X-ray in patients for non-cardiothoracic surgery is sensible, because patients with COPD are at increased risk of pulmonary neoplasm.

Evidence

Abnormal chest X-ray is predictive of perioperative pulmonary complications (defined as CXR showing hyperinflation, nodules or masses, hilar fullness, or interstitial changes): Level of Evidence: A; Strength of Recommendation: I (Kroenke, 1993).

COPD clients have an increased risk of pulmonary neoplasm: Level of Evidence: C; Strength of Recommendation: IIb (ATS, 1995).

F. Is $FEV_1 \leq 35$ Percent of Predicted?

Objective

To identify patients who are likely candidates for surgery based on pulmonary function tests.

Annotation

Severe COPD ($FEV_1 \leq 0.75$ L) is a predictor of prolonged ICU stay. FEV_1/FVC predicts postoperative complications. (See evidence for annotation D above)

G. Refer to Pulmonary Specialist

Objective

To determine when a pulmonary consult is indicated.

Annotation

Patients should be referred to a respiratory or thoracic specialist prior to scheduling of a lung resection. In some cases, for example in patients with mild COPD and a solitary pulmonary nodule, the patients can be referred directly to a thoracic surgeon.

H. Is $PaCO_2 \geq 45$?

Objective

To determine risk factors for postoperative pulmonary complications.

Annotation

Hypercapnia is an independent risk factor for patients with moderate to severe COPD who are having upper abdominal or thoracic surgery.

Evidence

$PaCO_2 \geq 45$ mmHg poses higher surgical risk: Level of Evidence: C; Strength of Recommendation: IIb (ATS, 1995).

A high $PaCO_2$ indicates a need for intense and careful preoperative support: Level of Evidence: C; Strength of Recommendation: IIb (Celli, 1993).

I. Is Surgery on Upper Abdomen or Thorax?

Objective

To determine which patients are at high risk for postoperative pulmonary complications based on type of surgery.

Annotation

The guidelines for the American Thoracic Society state that upper abdominal surgery poses a risk of postoperative pulmonary complications for all patients. Upper abdominal surgery shifts the respiratory pump from the diaphragm to the accessory muscles, due to a non pain-related reflex. Non imperative upper abdominal surgery such as cholecystectomy should be avoided in patients with moderate to severe COPD. If surgery is necessary, provide careful anesthesia. Another potential way to decrease operative risk may be to perform the procedure laparoscopically.

Evidence

Thoracic or upper abdominal surgery is high-risk in patients with moderate to severe COPD: Level of Evidence: C; Strength of Recommendation: I (ATS, 1995).

Shift in respiratory pump activity from the diaphragm to other muscles: Level of Evidence: C; Strength of Recommendation: I (Ford, 1993).

Upper abdominal incision is a risk factor for postoperative pulmonary complications: Level of Evidence: A; Strength of Recommendation: I (Hall, 1991).

J. Preoperative Management

Objective

To determine preventive measures for postoperative pulmonary complications.

Annotation

1. Counsel Tobacco Use Cessation

   There is evidence that stopping cigarette smoking two months before surgery reduces perioperative complications. For smokers quitting less than eight weeks preoperatively, no such evidence exists, but consensus exists that quitting even immediately before surgery could be beneficial.

Evidence

Stopping cigarette smoking 8 weeks preoperatively reduces pulmonary complications: Level of Evidence: C; Strength of Recommendation: IIb (Warner, 1989).

Every effort should be made to have the patient stop smoking: Level of Evidence: C; Strength of Recommendation: IIb (Celli, 1993).

2. Administer Postoperative Subcutaneous Heparin

   Postoperative subcutaneous heparin is useful for prophylaxis for pulmonary emboli, and should be considered strongly in patients who start with limited pulmonary reserve.

Evidence

Subcutaneous heparin reduces fatal pulmonary emboli: Level of Evidence: B; Strength of Recommendation: I (Collins, 1988).

3. Incentive Spirometry Respiratory Care

   Arrange for postoperative incentive spirometry or controlled deep breathing and cough.

   Deep breathing and controlled cough with or without incentive spirometry should be done postoperatively.

Evidence

Incentive spirometry can reduce hospital stay: Level of Evidence: C; Strength of Recommendation: I (ATS, 1995).

Algorithm A5

Outpatient Management of COPD: Management of Air Travel (Module A5)

A. Patient with Stable COPD Planning Air Travel

Objective

The algorithm employs the most practical and least invasive methods to apply current recommendations regarding oxygen supplementation during flight.

Annotation

Commercial airliners can cruise at altitudes over 40,000 feet with their cabins pressurized from 6,000 to 8,000 feet. This is equivalent to an inspired O_2 concentration at sea-level of about 15 percent. Patients with severe COPD experience falls in their PaO_2 that average 25 mmHg but may be more than 30 mmHg at 8,000 feet than at sea level. Since their sea level PaO_2 values are on the steep part of the oxygen-hemoglobin dissociation curve, the fall in SaO_2 with falls in PaO_2 may be quite sharp. Altitude PaO_2 is a commonly used marker to assess risk of air travel adverse effects on patients with COPD.

B. Is Patient Hypercapnic or On Long-Term Oxygen Therapy?

Objective

To identify patients at increased risk for adverse physiologic effects of altitude exposure and determine factors that may influence health risks of exposure to decreased PaO_2 during air travel.

Annotation

Identify patients who require specialist-level evaluation for advanced testing to determine whether supplemental oxygen is necessary and safe. Specialists will perform effective oxygen titration if required.

Evidence

Safety of air travel for cardiopulmonary patients with severe lung disease: Level of Evidence: B; Strength of Recommendation: IIb (Aerospace Medical Association [ASEM], 1996; Lien, 1998).

Prediction of Altitude hypoxemia in COPD: Level of Evidence: B; Strength of Recommendation: IIb (Dillard, 1989, 1993, 1995; Gong, 1984; Naughton, 1995).

Morbidity and mortality during air travel: Level of Evidence: B; Strength of Recommendation: IIb (Cummins & Shuback, 1989; Speizer, 1989).

C. Obtain Calculated Predicted PaO_2 During Flight

Objective

To determine whether the patient is at increased risk for potentially physiologically significant hypoxemia in a pressurized commercial aircraft.

Annotation

As noted in Annotation A above, predicted altitude hypoxemia serves as a parameter for decision-making regarding oxygen supplementation during air travel for ambulatory patients with stable COPD. Prediction of altitude-induced hypoxemia can be accomplished by several methods. Regression equations have been validated for this purpose. Individual variability in the populations studied for development of prediction equations limits the applicability of the results in clinical decision making for patients with borderline values of predicted PaO_2 at altitude. Individualized hypoxia inhalation testing is advised for these patients to determine whether supplemental oxygen therapy is advised during air travel. Hypobaric chamber testing, face mask hypoxic gas inhalation, Venturi mask nitrogen enriched gas, and normobaric hypoxic gas chamber methods have all been utilized for this purpose. Hypoxic gas mixture testing by face mask delivery has been shown to yield similar PaO_2 decrements similar to those in hypobaric chamber testing, as has normobaric hypoxic gas chamber exposure. These specialized hypoxia simulation studies are available in appropriately equipped laboratories and are usually conducted under the direction of a pulmonary specialist.

Regression equation predictions are applicable to the majority of COPD patients. These equations apply only to non-hypercapnic patients. There is good agreement between the regression equations. The PaO_2 at sea level (PaO_2SL), FEV_1 percent predicted, and FEV_1/FVC ratio are the best independent predictors of the PaO_2 during hypobaric chamber or hypoxic gas inhalation testing (PaO_2Alt), according to the following equation:

$$PaO_2 \text{ Alt mmHg} = 0.453\ [PaO_2SL \text{ mmHg}] + 0.386\ [FEV_1 \text{ \% pred}] + 2.44$$
$$(r = 0.847,\ p < 0.0001)$$

Since FEV_1percent predicted and FEV1/FVC influence PaO_2Alt, it is important to optimize FEV_1 by pharmacotherapy before and during air travel. Table I provides the calculated values of PaO_2Alt for given values of PaO_2SL in the range of 60 to 80 mmHg. If the PaO_2 is > 80, the patient probably does not need oxygen for travel.

Table. Predicted in flight PaO_2 based on PaO_2 at Sea Level and FEV_1

FEV_1 % Predicted		100	90	80	70	60	50	
PaO_2 at sea level	80	56.2	54.9	52.7	50.9	49.2	47.4	
	70	51.6	49.9	48.1	46.4	44.6	42.9	
	60	47.1	45.4	43.6	41.9	40.1	38.4	

Evidence

Predicting PaO_2 at altitude from PaO_2 at ground level. Methods: Breathing Hypoxic gas mixtures at SL; exposure to simulated altitude in hypobaric

chamber: Level of Evidence: B; Strength of Recommendation: IIb (Dillard, 1989, 1993, 1995; Gong, 1984; Naughton, 1995).

D. Is predicted PaO2 $\leq$55?

Objective

To identify appropriate dosing, titration, and delivery of supplemental oxygen for patients to minimize altitude hypoxemia-related health risks and avoid potential adverse effects of increased oxygen concentration for hypercapnic patients.

Annotation

Supplementation of oxygen for COPD patients who are eucapnic and without cardiac or cerebrovascular disease has been studied in several hypoxic environments with multiple delivery systems. Nasal cannula (NC) and Venturi masks in a hypobaric chamber, NC in hypoxic gas inhalation trials, and NC in a normobaric hypoxic chamber have all been investigated. The sum of these studies suggests that most patients with moderate to severe COPD will have PaO_2 values above 60 mmHg or 90 percent saturation by pulse oximetry with 1 to 3 liters of NC oxygen supplementation during simulated aircraft cabin environmental exposure. When practical, a supplementation trial by one of these methods can be used to individualize dosing of oxygen. Empiric dosing of two liters by NC utilizes commonly available equipment and will allow an adequate supply for all but long-haul flights, with maintenance of $PaO_2 \geq$ 60 mmHg for most patients.

A patient's PaO_2 during commercial air travel predicted by regression equations to be borderline (51 to 54) should be individually evaluated. Individual variability in the populations studied for development of prediction limits the applicability of the results for clinical decision making in patient with "borderline" values of predicted PaO_2 at altitude. Individualized hypoxia inhalation testing is advised for these patients, to determine if supplemental oxygen therapy is advisable during air travel. Hypobaric chamber testing, face mask hypoxic gas inhalation, Venturi mask nitrogen enriched gas, and normobaric hypoxic gas chamber methods have all been utilized for this purpose. Hypoxic gas mixture testing by face mask delivery has been show to be cause similar PaO_2 decrements as hypobaric chamber testing, similar to those in normobaric hypoxic gas chamber exposure.

Patients with hypercapnia have not been included in the patient populations from which prediction equations were developed. Therefore, these patients require individualized hypoxia testing to determine whether supplemental oxygen is advised. If so, careful titration of the additional flow rate should be accomplished prior to flight, with attention to the effect on ventilation. Specialized testing and titration of oxygen should be accomplished in an appropriately equipped laboratory with specialist supervision.

Evidence

Published evidence regarding oxygen supplementation during flight: Level of Evidence: B; Strength of Recommendation: IIb (Berg, 1992; Vohra, 1993; Cramer, 1996).

E. Oxygen Supplementation Recommendations for Patients without Hypercapnia, Cerebrovascular Disease, or Cardiovascular Disease

Objective

To identify patients at low risk and those at increased risk for adverse physiological effects of altitude exposure.

Annotation

Some authors have chosen a predicted altitude PaO_2 of 50 mmHg as the threshold below which supplementary oxygen should be prescribed. However, this value is arbitrary, with no outcome studies to support it. Many eucapnic COPD patients are well acclimated to hypoxemia and in altitude simulation tests, many stable eucapnic patients with COPD and no known heart disease are relatively asymptomatic at rest. They do not experience cardiac arrhythmias and have good short-term tolerance to PaO_2 values of 35 to 40 mmHg. Exercise in this environment however, causes a further decline in PaO_2. Thus, the advising physician must still rely largely on clinical evaluation, judgment, and a history of successful flights in advising each patient who wishes to fly. Several published recommendations suggest that stable COPD patients without cardiac or cerebrovascular disease who are predicted to have a $PaO_2 \leq$ 50mmHg during flight require supplemental oxygen. These recommendations seem practical, and prudent.

There is no recommendation or evidence suggests that stable COPD patients without cardiac or cerebrovascular disease who are predicted to have a $PaO_2 \geq$ 50mmHg during flight require supplemental oxygen. Because of considerable individual variability in the prediction equation, a threshold of 55 mmHg for this method is advised as a lower-limit threshold for this recommendation. Patients with a predicted PaO_2 of 51 to 54 by regression equation should therefore undergo individualized testing to determine their predicted altitude PaO_2.

Evidence

Published recommendations regarding oxygen supplementation thresholds: Level of Evidence: B; Strength of Recommendation: IIb (Gong, 1992; Lien, 1998; Aerospace Medical Association [ASEM], 1996.

Algorithm A6

Outpatient Management of COPD: Insomnia (Module A6)

A. Institute Sleep Hygiene Measures

Objective

To educate the patient regarding proper sleep hygiene.

Annotation

Institute sleep hygiene measures

1. Homeostatic drive for sleep:
    a. Avoid naps.
    b. Too much time in bed can decrease sleep quality on the subsequent night.
    c. Exercise each day. It is best to finish exercise at least six hours before bedtime.
    d. Take a hot bath for 30 minutes within two hours before bedtime. A hot drink may help you relax as well as warm.
2. Circadian factors:
    a. Keep a regular rising time seven days a week.
    b. Do not expose yourself to bright light if you have to get up at night.
    c. Get at least one-half hour of sunlight within 30 minutes after arising.
3. Drug effects:
    a. Evaluate patient medication profile for drug likely to cause insomnia (beta2-agonists, theophylline, oral steroids).
    b. Stop tobacco use.
    c. Avoid caffeine entirely for a 4-week trial period; limit caffeine use to no more than three cups before 10 a.m. if caffeine cannot be stopped.
    d. Avoid alcoholic beverages before bedtime.
4. Arousal in sleep setting:
    a. Keep clock face turned away, and do not find out what time it is when you wake up at night.
    b. Avoid strenuous exercise after six p.m.
    c. Avoid eating or drinking heavily for three hours before bedtime. A light bedtime snack may help.
    d. If you have trouble with regurgitation, be especially careful to avoid heavy meals and spices in the evening. Do not retire too hungry or too full. Head of bed may need to be raised.
    e. Keep your room dark, quiet, well ventilated, and at a comfortable temperature throughout the night. Ear plugs and eyeshades are OK.
    f. Have a non stressful bedtime ritual.
    g. Set aside a worry time other than bedtime.
    h. Do not try too hard to sleep; instead, concentrate on the pleasant feeling of relaxation.
    i. Use stress management in the daytime.
    j. Avoid unfamiliar sleep environments.
    k. Be sure the mattress is not too soft or too firm, and the pillow is of the right height and firmness.
    l. An occasional sleeping pill probably is acceptable.
    m. Use the bedroom only for sleep or sex; avoid other activities that lead to prolonged arousal.

Evidence

ASDA Practice Parameters for Indications for Polysomnography: Level of Evidence: B; Strength of Recommendation: I (American Sleep Disorders Association [ASDA], 1997).

ASDA nosology of sleep disorders: Level of Evidence: B; Strength of Recommendation: I (ASDA, 1990).

Sleep hygiene: Level of Evidence: C; Strength of Recommendation: I (Zarcone, 1994).

B. Initiate a Trial of Zolpidem (5mg/qhs)

Objective

To determine the effects of a therapeutic trial with zolpidem.

Annotation

Hypnotics should be used only after other measures have been tried (see Annotation A above) and should be used sparingly with close attention to the possibility of abuse and untoward side effects. If the decision is made to use a hypnotic, zolpidem is the first choice in patients with moderate/severe COPD (FEV_1 < 50 percent predicted; $SaO_2 \leq$ 90 percent; and CO_2 retention) since it has generally been shown to be safe when given repeatedly in these patients. If the patient snores habitually, all hypnotics must be used with great caution, as they may induce or exaggerate sleep apnea and hypopnoia, even in asymptomatic patients. If zolpidem 5mg/qhs is not effective, the dose may be increased to 10mg/qhs.

C. Initiate a Trial of Triazolam (0.125 mg/qhs)

Objective

To determine the therapeutic effects of a trial with triazolam.

Annotation

Hypnotics may have adverse effects for patients with moderate to severe COPD. Triazolam has no obvious effect on respiration when used in single doses for patients with an awake supine $SaO_2 \geq$ 90 percent and no carbon dioxide retention ($PaCO_2 \leq$ 45), and may be considered in addition to zolpidem in such patients. If the patient has supine $SaO_2 \leq$ 90 percent, zolpidem is clearly the first choice; triazolam and other benzodiazepines must be used with extreme caution. Other short-acting benzodiazepines (e.g., temazepam) may substitute for triazolam based on availability, cost, and experience of the practitioner.

Evidence

Hypnotic use of single and multiple doses of 10 mg zolpidem is safe and efficacious in stable patients with severe COPD (mean FEV_1 0.84L): Level of Evidence: B; Strength of Recommendation: I (Girault, 1996).

Hypnotic use of single doses of 0.125 and 0.25 mg of triazolam is safe and efficacious in stable COPD patients without significant hypoxemia or CO_2 retention: Level of Evidence: B; Strength of Recommendation: I (Timms, 1988).

Triazolam and zolpidem are safe in patients with mild COPD (mean FEV_1 62% predicted): Level of Evidence: B; Strength of Recommendation: I (Steens, 1993).

Flunitrazepam produced a reduction in PaO_2 and an increase in $PaCO_2$; Triazolam decreased minute ventilation; Zolpidem produced no significant changes in awake patients with very severe COPD (mean FEV_1 32% predicted): Level of Evidence: B; Strength of Recommendation: I (Murciano, 1993).

D. Follow-Up with Routine Care
    1. Refer to respiratory specialist if symptoms do not resolve as expected, if there are complications limiting therapy or if these recommendations do not readily apply to the patient.
    2. If general measures and occasional hypnotics are unsuccessful, referral to a psychiatrist or sleep specialist.

Algorithm B1

Inpatient Management of COPD: Emergency Room and Hospital Ward Management (Module B1)

A. Patient Presents With Acute Exacerbation of COPD

Definition

An acute exacerbation of COPD is defined as an acute clinical deterioration in a patient's respiratory status due to a worsening of the underlying COPD. Symptoms and signs of acute exacerbation of COPD include:

1. Increased dyspnea
2. Tachycardia
3. Increased cough
4. Increased sputum production
5. Change in sputum color or character
6. Accessory muscle use
7. Peripheral edema
8. Development of or increase in wheeze
9. Loss of alertness
10. Loss of energy
11. Fever
12. Increased respiratory rate

13. Decrease in FEV_1 or peak expiratory flow
14. Worsening of arterial blood gases or pulse oximetry
15. Chest tightness

Evidence

Definition of acute exacerbation: Level of Evidence: C; Strength of Recommendation: IIa (Siafakas, 1995; BTS, 1997).

B. Does Patient Need Mechanical Ventilation?

Objective

To initiate immediate action for a patient with life-threatening acute respiratory failure due to acute exacerbation of COPD.

Annotation

Decision to initiate mechanical ventilation and tracheal intubation can be made prior to obtaining arterial blood gases. Advance directives should be considered prior to initiating these supportive measures.

1. Indications for mechanical ventilation (invasive or noninvasive/BiPAP) include:
    a. Severe respiratory or combined respiratory and metabolic acidosis
    b. Sustained respiratory rate $\geq$ 40 per minute
    c. Abnormal breathing pattern suggestive of increased respiratory workload and/or respiratory muscle fatigue
    d. Depressed mental status
    e. Severe hypoxemia
2. Indications for tracheal intubation include:
    a. Suspected airway obstruction
    b. Depressed mental status
    c. High risk of gastropulmonary reflux and aspiration
    d. Difficulty managing secretions

Evidence

Mechanical ventilation and endotracheal intubation: Level of Evidence: C; Strength of Recommendation: I (ATS, 1995).

C. Ventilate and Perform Cardiopulmonary Resuscitation (CPR) as Indicated

Objective

To initiate immediate action for a patient who presents with life threatening acute respiratory failure due to acute exacerbation of COPD.

Annotation

CPR should be performed according to Advanced Cardiac Life Support (ACLS) protocol. A physician with special expertise in critical care medicine should be consulted at this point. Care should be used to avoid complications of auto positive end-expiratory pressure (PEEP) and acute respiratory alkalosis.

D. Perform Clinical and Laboratory Evaluation

The critical elements of the clinical evaluation, adapted from both the ATS and ERS guidelines, include:

1. History:
    a. Baseline respiratory status
    b. Sputum volume and characteristics
    c. Cough
    d. Duration and progression of symptoms
    e. Dyspnea severity
    f. Exercise limitations
    g. Sleep and eating difficulties
    h. Home care resources
    i. Home therapeutic regimen
    j. Symptoms of comorbid acute and chronic conditions
2. Clinical assessment:
    a. Temperature
    b. Respiratory rate
    c. Heart rate
    d. Cyanosis
    e. Accessory muscle use
    f. Edema
    g. Cor pulmonale
    h. Bronchospasm
    i. Hemodynamic instability
    j. Altered mentation
    k. Paradoxical abdominal retractions
    l. Use of accessory respiratory muscles
3. Spirometry (optional):
    a. Peak expiratory flow rate
    b. FEV_1
4. Laboratory:
    a. ABG
    b. Chest radiograph
    c. EKG
    d. Theophylline level (if applicable)
    e. WBC count
    f. Blood cultures if pneumonia
    g. Electrolytes
    h. BUN
    i. Glucose

Evidence

Comorbid conditions: Level of Evidence: C; Strength of Recommendation: I (Siafakas, 1995).

Clinical and laboratory evaluation: Level of Evidence: C; Strength of Recommendation: I (ATS, 1995; Siafakas, 1995).

E. Complete Evaluation and Treatment of Comorbid Conditions and Other Factors Contributing to Exacerbation

Objective

To identify comorbid conditions that are likely in patients with COPD, and might contribute to acute exacerbation and for which specific interventions should be considered.

Annotation

Comorbid conditions that may impact upon the treatment of exacerbation of COPD include the following, which were adapted and modified from ERS table:

1. Congestive heart failure or disturbances in cardiac rhythm
2. Pneumonia
3. Pulmonary embolism
4. Spontaneous pneumothorax
5. Inappropriate oxygen therapy
6. Psychotropic drugs (hypnotics, tranquilizers, narcotics, etc.)
7. Drug allergy (penicillin, cephalosporin, etc.)
8. Metabolic disease (diabetes mellitus, electrolyte disorders such as hypophosphatemia, hypokalemia)
9. Poor nutritional status
10. Myopathy
11. Other acute illness (acute abdomen, GI hemorrhage, CVA, etc.)
12. Systemic use of corticosteroids

Some of these comorbidities will require hospitalization.

Evidence

Comorbid conditions: Level of Evidence: C; Strength of Recommendation: I (Siafakas, 1995).

F. Admit to ICU

Objective

To provide direct observation and 24-hour monitoring for patient with severe exacerbation.

Annotation

ICU patients are treated the same as ward patients except for cardiopulmonary monitoring and direct observation. A specialist in critical care medicine should be consulted for these patients.

G. Does Patient Meet ICU Admission Criteria?

Objective

To identify patients who will benefit from special care.

Annotation

Any of the following would prompt admission to the ICU for closer observation and monitoring (adapted and modified from American Thoracic Society guidelines).

1. Severe dyspnea that responds inadequately to initial emergency room therapy
2. Confusion, lethargy, or respiratory muscle fatigue
3. Persistent or worsening hypoxemia despite supplemental O_2 or severe or worsening of respiratory acidosis ($pH \leq 7.30$)
4. Required assisted mechanical ventilation, whether through means of tracheal intubation or noninvasive techniques

Evidence

ICU admission criteria: Level of Evidence: C; Strength of Recommendation: IIa (ATS, 1995).

H. Does Patient Meet Discharge Criteria?

Objective

To establish criteria for discharge from the emergency room.

Annotation

Discharge criteria for patients with acute exacerbation of COPD (adapted and modified from American Thoracic Society guidelines):

1. Features of the severe exacerbation are resolved (see Annotation D in the Core Module above).
2. Anticipated need for inhaled bronchodilators is not more frequent than every 4 hours and the patient is on oral medication.
3. Reversible component of airway obstruction, if present, is under stable control.
4. Patient or caregiver understands appropriate use of medications.
5. Follow-up and home care arrangements have been completed (e.g., visiting nurse, oxygen delivery, meal provisions).
6. Patient, family, and physicians are confident that the patient can manage successfully.

Evidence

Discharge criteria: Level of Evidence: C; Strength of Recommendation: I (ATS, 1995).

I. Admit to Ward

Objective

To establish criteria for admission to a general medical ward for acute exacerbation of COPD.

Annotation

Indications for hospitalization of patients with COPD (adapted and modified from American Thoracic Society guidelines):

1. Patient has acute exacerbation plus one or more of the following:
    a. Inadequate response of symptoms to outpatient management
    b. Inability to walk between rooms (patient previously mobile)
    c. Inability to eat or sleep due to dyspnea
    d. Conclusion by family and/or physician that patient cannot manage at home and supplementary home care resources are not immediately available
    e. A high-risk comorbid condition, pulmonary (e.g., pneumonia) or non pulmonary
    f. Prolonged, progressive symptoms before emergency department visit
    g. Altered mentation
    h. Worsening hypoxemia
    i. New or worsening hypercarbia
2. Patient has new or worsening cor pulmonale unresponsive to outpatient management
3. A planned invasive surgical or diagnostic procedure requires analgesics or sedatives that may worsen pulmonary function
4. Comorbid conditions (e.g., steroid myopathy or vertebral compression fractures) have worsened pulmonary function

Other indications for hospitalization may apply to patients undergoing pulmonary rehabilitation.

Evidence

Ward admission criteria: Level of Evidence: C; Strength of Recommendation: IIa (ATS, 1995).

J. Is Patient Improving?

Objective

To establish criteria for measuring a favorable response to treatment.

Annotation

Improvement is indicated by:

1. Reduced dyspnea
2. Decreased respiratory rate
3. Improved air movement
4. Decreased use of accessory muscles
5. Improved peak expiratory flow
6. Improved FEV_1 and/or ABGs

K. Continue Treatment

Objective

To establish guidelines for tapering treatment for patients who are improving.

Annotation

1. Decrease frequency of inhaled beta2-agonists to every 4 to 6 hours (see Module B3 below)
2. Switch to MDI with spacers
3. Switch from parenteral to oral medication
4. Titrate oxygen as per oxygen protocol (see Module B3 below)

L. Intensify Treatment

Objective

To establish guidelines for treating patients who fail to respond to the initial therapy (e.g., intensification of the management regimen).

Annotation

1. Consider using aerosol beta-agonists if MDI cannot be used effectively. (see Module B3 below).
2. Consider using IV steroids and/or antibiotics (see Module B3 below).
3. Titrate oxygen, using oxygen therapy (see Module B4 below).
4. Consider comorbidities or other contributory causes of COPD and treat.

M. Reassess in 30 Minutes - Consider Specialist Consultation

Objective

To establish criteria for consultation by a specialist in chest medicine.

Annotation

1. Patients who require more intensive treatment but do not require ICU admission should be considered for consultation with a pulmonary specialist.
2. Repeated intensification of treatment without improvement would warrant consultation with a pulmonary specialist.

Algorithm B2

Inpatient Management of COPD: Pharmacotherapy (Module B2)

A. Can Patient Effectively Use Metered Dose Inhaler (MDI) with Spacer?

Objective

To establish guidelines for the appropriate use and dosing of inhaled bronchodilators in the in-patient setting and to establish criteria for the use of a small-volume nebulizers (SVN) versus metered dose inhaler (MDI) with spacer in the hospital setting.

Annotation

Selective $beta_2$-adrenergic agonists are first-line agents:

1. Aerosolization using a low-volume nebulizer is generally the first mode used when the patient is severely dyspneic.
2. After the patient has stabilized and can use the MDI, there is no difference between using an MDI with a spacer and nebulized aerosolization.
3. An optimal dosing schedule of beta2-agonists cannot be suggested.
4. Beta2-agonists should be titrated to maximal effect.
5. Monitor closely for adverse effects of the larger-than-usual doses that are sometimes necessary to relieve airway obstruction.

Selective beta2-agonists are less likely to cause tachycardia.

Nebulizer aerosolization is used when the patient is severely dyspneic and can neither effectively breathe nor coordinate for effective MDI use. After the patient has stabilized and can use the MDI, there is no difference between using an MDI with a spacer compared with nebulized aerosolization. The patient's skill with MDI should be evaluated by demonstration.

No large, well-done, randomized, placebo-controlled clinical trials have been conducted. Therefore, an optimal dosing schedule of beta2-agonists cannot be suggested. Beta2-agonists should be titrated to maximum effect when possible, monitoring closely for adverse effects of the larger-than-usual doses that are sometimes necessary to relieve airway obstruction. Beta2-agonists have a reduced functional half-life in exacerbation of COPD and therefore, if tolerated, may be given every 30 to 60 minutes under close supervision (including EKG monitoring). High-dose beta2-agonist treatment regimens have not been investigated widely in this patient population and should be used cautiously until results of more controlled clinical trials are available.

Table. Medication for Acute Exacerbation of COPD

Medication	MDI Dose	Nebulizer Dose	Specia Instructi

Short Acting $Beta_2$ Agonists			
Albuterol	3-4 puffs q½-2 h	2.5 mg q½-2 h	Deliver medic with nebulizer unable to use with spacer (1
Metaproterenol	3-4 puffs q½-2 h	10-15 mg q½-2 h	
Terbutaline	3-4 puffs q½-2 h	N/A	
Anticholinergics			
Ipratropium Bromide	3-6 puffs q2-4h	500 micrograms q2-4h	
Systemic Steroids	Intravenous		
Solumedrol	125 mg q6h x 72 hours		Taper schedul • Da 60 mg ora prednison • Da 11: 40mg prednison • Da 15: 20 m prednison
	Oral		
Prednisone	40-60 mg q day		Taper off or cl qod within 1 t weeks
Prednisilone	30-50 mg q day		
Theophylline	If on theophylline check level		Aim for levels 12 microgram

Evidence

Beta2-agonists use in AECOPD: Level of Evidence: A; Strength of Recommendation: I (Rebuck et al., 1987; Carpel et al., 1990)

Use nebulizer or MDI with spacer in AECOPD: Level of Evidence: A; Strength of Recommendation: IIa (Turner, 1988; Berry et al., 1989; Maguire et al., 1991; Jasper, 1987).

Give beta2-agonists every 30 to 60 minutes if tolerated in AECOPD: Level of Evidence: C; Strength of Recommendation: I (ATS, 1995).

B. Administer Corticosteroids

Objective

To establish criteria for the use of corticosteroids.

Annotation

Steroids should be given early in patients with acute exacerbation (AE) of COPD. Studies demonstrating the benefits of corticosteroids in AE involved a small number of patients and show small improvement in lung function. A VA cooperative trial (the SCCOPE trial) addressed the role of corticosteroids in AE, presented at an American Thoracic Society meeting in 1998 indicating a benefit from the use of steroids in this clinical situation. We believe corticosteroids are of benefit in AE and should be given early, particularly in patients with severe underlying lung function and in those with severe exacerbation. The recommend dose equivalents of at least 0.5 mg/kg of methylprednisolone every 6 hours for at least 3 days.

Evidence

Budesonide with oral prednisone: Level of Evidence: A; Strength of Recommendation: I (Morice et al., 1996).

Corticosteroids: Level of Evidence: A; Strength of Recommendation: I (Neiwohner et al., 1999).

Methylprednisolone: Level of Evidence: B; Strength of Recommendation: I (Emerman et al., 1989).

Methylprednisolone: Level of Evidence: A; Strength of Recommendation: I (Albert et al., 1980).

Oral prednisone: Level of Evidence: A; Strength of Recommendation: I (Thompson et al., 1996).

Oral Prednisone: Level of Evidence: A; Strength of Recommendation: I (Neiwohner et al., 1999).

C. Consider Other Drug Therapies or Treatments as Indicated

Objective

To identify the role of anticholinergic agents, theophylline, other pharmacologic agents, and miscellaneous adjunctive agents/therapies.

Annotation

0. Anticholinergic agents may be valuable as additive or single agents particularly if the patient is intolerant of beta2-agonist or has side effects, have significant coronary artery disease or severe left ventricular dysfunction.
   High-dose ipratroprium bromide, although possibly effective, has not been studied in acute exacerbation of COPD. If the decision to use ipratropium is made, the following dose is suggested: 500 micrograms every six hours by nebulizer, or six to eight puffs every four hours by MDI with spacer.
1. Theophylline Use: There is inadequate evidence in the literature to recommend the routine use of theophylline or amce to exclude a benefit for selected patients. Toxicity occurs frequently in hospitalized patients and is associated with a prolonged stay. Clinicians who choose to use this agent must be thoroughly familiar with its metabolism, drug interactions, and toxicity.
2. Other Parenteral Agents: Parenteral administration of terbutaline or epinephrine has a prompt effect but is accompanied by an increased risk for tachycardia and may be more arrhythmogenic when compared with the inhaled route in theophylline in treatment of acute exacerbation of COPD. However, there is also inadequate evidence. Since an increased potential for myocardial ischemia is an unintended consequence of parenteral adrenergic use, it cannot be recommended in adult patients with COPD. This is a particular concern in patients in whom cigarette use is a potent risk factor for both COPD and coronary artery disease. Terbutaline and epinephrine are not recommended.
3. Additional Therapies Treatment Considerations: The following measures lack adequate evidence to support their routine use in the management of acute exacerbation of COPD: directed coughing, chest physiotherapy, positive end-expiratory pressure, nasotracheal suctioning, systemic hydration beyond replacement to euvolemia, intermittent positive pressure breathing, bland aerosol therapy and mucolytic therapy. Further research is indicated in these areas.

   The nutritional status of the patient is another important consideration. Care must be exercised so that patients receive adequate and appropriate nutrition during their stay. Also, patients should be encouraged to mobilize as soon as is practical. When confined to bed, range-of-motion exercises should be performed. Consider deep-vein thrombosis prophylaxis.

Evidence

Additive effect of B_2-agonists and ipratroprium bromide in AECOPD: Level of Evidence: A; Strength of Recommendation: IIa (Chapman et al., 1985; Shrestha et al., 1991; Rebuck et al., 1987; O'Driscoll et al., 1989; Karpel et al., 1990).

Ipratroprium bromide alone is effective in acute exacerbation of COPD: Level of Evidence: A; Strength of Recommendation: I (Rebuck et al., 1987; Karpel et al., 1990; Lloberes et al., 1988).

Aminophylline: Level of Evidence: B; Strength of Recommendation: IIb (Rice et al., 1987; Wrenn et al., 1991).

Other parenteral agents: Level of Evidence: C; Strength of Recommendation: II (ATS, 1995).

Directed coughing: Level of Evidence: C; Strength of Recommendation: IIa (ATS, 1990, 1991, 1995).

Chest physiotherapy, percussion and vibration, postural drainage: Level of Evidence: C; Strength of Recommendation: IIb (ATS, 1990, 1991, 1995).

Positive end-expiratory pressure: Level of Evidence: C; Strength of Recommendation: IIb (ATS, 1995).

Nasotracheal suctioning (non-intubated): Level of Evidence: C; Strength of Recommendation: IIb (ATS, 1990, 1991, 1995).

Mini-tracheotomy: Level of Evidence: C; Strength of Recommendation: IIb (ATS, 1995).

Systemic hydration to euvolemia: Level of Evidence: C; Strength of Recommendation: I (ATS, 1990, 1991, 1995).

Intermittent positive pressure breathing: Level of Evidence: C; Strength of Recommendation: II (ATS, 1995).

Bland aerosol therapy: Level of Evidence: C; Strength of Recommendation: IIb (ATS, 1995).

Mucolytics: Level of Evidence: C; Strength of Recommendation: IIb (ATS, 1995).

Relaxation techniques: Level of Evidence: C; Strength of Recommendation: IIb (Siafakas, 1995; ATS, 1990, 1991).

Control of breathing, pursed lip breathing, diaphragmatic breathing: Level of Evidence: C; Strength of Recommendation: IIb (Siafakas, 1995; ATS, 1990, 1991).

Nutritional intervention to achieve ideal body weight: Level of Evidence: C; Strength of Recommendation: IIa (ATS, 1995; Siafakas, 1995).

D. Consider Antibiotics

Objective

To identify criteria for using antibiotics in the treatment of acute exacerbation of COPD.

Annotation

Many patients with AE do well without antibiotic treatment. However, for patients whose exacerbation is associated with changes in sputum (quality, volume, color) or fever, antibiotics are a reasonable treatment option. Patients who are older than 60 years or have severe underlying lung function are more likely to benefit from the use of antibiotics. In most studies, the choice of antibiotic was not important. Usually, the older, less expensive antibiotics, such as amoxicillin, trimethoprim-sulfamethoxazole, and doxycycline, will suffice. However, the choice may be affected by the history of exacerbation in the individual patient and by the pattern of microbial resistance found in the community. It is important to keep the possibility of drug interactions in mind when selecting antibiotics. This should be a consideration for any patient on theophylline.

Evidence

Antibiotics should be used in acute exacerbation of COPD with change in phlegm: Level of Evidence: A; Strength of Recommendation: IIa (Anthonisen et al., 1987; Pines, 1968; Saint et al., 1995).

Use antibiotics for severe exacerbation only: Level of Evidence: A; Strength of Recommendation: IIa (Anthonisen et al., 1987; Balter et al., 1994; ATS, 1995).

E. Has the Patient's Respiratory Status Improved?

Objective

To establish criteria for measuring a favorable response to treatment.

Annotation

Improvement is indicated by:

0. Reduced dyspnea
1. Decreased respiratory rate
2. Improved air movement
3. Decreased use of accessory muscles
4. Improved peak expiratory flow, improved FEV_1 and/or ABGs

Improvement is indicated by reduced dyspnea, decreased respiratory rate, improved air movement, and decreased use of accessory muscles. Objective measures such as peak expiratory flow, FEV_1, and/or ABGs should demonstrate improvement. An elevated heart rate may indicate beta2-agonist toxicity.

F. Modify Treatment. Consider Tapering Medication

Objective

To establish guidelines for tapering treatment for patients who are improving.

Annotation

0. Decrease frequency of inhaled beta2-agonists to every four to six hours
1. Switch to MDI with spacers
2. Switch from parenteral to oral medication
3. Titrate oxygen per oxygen protocol (see Module B3 below)

G. Intensify Treatment

Objective

To establish guidelines for the treatment of patients who fail to respond to the initial therapy (e.g., intensification of the management regimen).

Annotation

0. Consider using aerosol beta2-agonists if MDI cannot be used effectively.
1. Consider using IV steroids and/or antibiotics.
2. Titrate oxygen, using oxygen therapy (see Module B3 below).
3. Consider comorbidities or other contributory causes of COPD and treat.

Optimal dosing schedules for beta2-agonists cannot be recommended due to the lack of acceptable placebo-controlled clinical trials. However, beta2-agonists should be titrated to maximal effect when possible, monitoring closely for adverse effects of the larger-than-usual doses that are sometimes necessary to relieve airway obstruction. Beta2-agonists have a reduced functional half-life in exacerbation of COPD and therefore, if tolerated, may be given every 30 to 60 minutes under close supervision (including EKG monitoring). High-dose beta2-agonist treatment regimens have not been investigated widely in this patient population and should be used cautiously until results of better controlled clinical trials are available.

Algorithm B3

Inpatient Management of COPD: Oxygen Therapy (Module B3)

The American Thoracic Society and European Respiratory Society guidelines were relied upon in devising this algorithm. A paucity of well-designed trials in this area mandated the use of consensus.

A. Using Oximetry, Titrate O_2 by Venturi Mask or Nasal Cannula (24 to 35 Percent) to 35 to an SaO_2 of 90 Percent

Objective

To delineate general principles of oxygen administration in patients with acute exacerbation of COPD.

Annotation

The goal of oxygen therapy is to optimize oxygenation and minimize respiratory acidosis, if present. Thus, all patients presenting with acute exacerbation of COPD should receive oxygen by Venturi mask (24 to 35 percent), which delivers a precise oxygen concentration, until the $PaCO_2$ is determined. The lowest fraction of inspired oxygen (FiO_2) resulting in an SaO_2 of 90 percent is optimal. The nasal cannula is to be avoided initially because of its inability to deliver a precise FiO_2. ABGs should be obtained initially and SaO_2 should be monitored continuously. If a ventilator is used in the ER, the initial FiO_2 setting should be 1.0.

B. Obtain ABGs

Objective

To emphasize the role of ABG determination in the initial management of patients with acute exacerbation of COPD and to define the role and limits of pulse oximetry in this setting.

Annotation

Analysis of ABGs is to be used initially in all cases when it is unknown whether the patient is a chronic CO_2 retainer and to determine acid-base status. Pulse oximetry, which should be continuously monitoring SaO_2, is not sufficient until it is clear that the CO_2 level is not elevated or is stable and the acid-base status is known and is stable.

C. Does Patient Need Mechanical Ventilation?

Objective

To define the guidelines for life saving mechanical ventilation and endotracheal intubation.

Annotation

A decision to initiate mechanical ventilation and endotracheal intubation can be made prior to measuring arterial blood gases. Advance directives should be considered prior to initiating these supportive measures.

1. Indications for mechanical ventilation (invasive or non invasive) include:
   Severe respiratory or combined respiratory and metabolic acidosis.
   a. Sustained respiratory rate greater than 40 per minute
   b. Abnormal breathing pattern suggestive of increased respiratory workload and/or respiratory muscle fatigue.
   c. Depressed mental status
   d. Severe hypoxemia
2. Indications for tracheal intubation include:
   a. Suspected airway obstruction

b. Depressed mental status
c. High-risk of gastro-pulmonary reflux and aspiration
d. Difficulty managing secretions

Evidence

Mechanical ventilation and endotracheal intubation: Level of Evidence: C; Strength of Recommendation: I (ATS, 1995).

D. Stepwise Increase in FiO_2

Objective

To encourage the use of a high flow controlled oxygen source in an acute exacerbation of COPD when $PaCO_2$ is suspected to be elevated.

Annotation

An SaO_2 of 90 percent is optimal. This usually corresponds to a PaO_2 of 55 to 60 mmHg. Pulse oximetry alone may be used in this situation once it is clear that $PaCO_2$ is not elevated and acid-base status is known and stable. Use of a Venturi mask, with analysis of arterial blood gases after 20 minutes (earlier if indicated clinically), is the most judicious approach to the management of acute exacerbation of COPD with oxygen in a patient having an elevated $PaCO_2$. If chronic elevation of $PaCO_2$ is not demonstrated and repeated measurement of acid base status is not a clinical concern, pulse oximetry alone to assess adequacy of oxygenation is acceptable, as is the use of nasal prongs or a cannula to deliver oxygen. However, when CO_2 retention exists, or when the acid-base status is unclear, assessment of $PaCO_2$ and pH are required. Use of pulse oximetry alone in this situation is to be avoided.

E. Are ABGs Acceptable?

Objective

To establish goals for PaO_2 and pH in patients with acute exacerbation of COPD.

Annotation

Acceptable blood gases would include a PaO_2 close to 60 mmHg, a stable $PaCO_2$, and a pH $\geq$ 7.25.

F. Decrease FiO_2 Progressively, Keeping PaO_2 or SaO_2 at 90 Percent AND Monitor Oximetry and ABGs

Objective

To delineate the salient points of oxygen administration in patients with elevated $PaCO_2$.

Annotation

Monitor with oximetry or ABGs. If CO_2 retention has been worsened by the use of a high concentration of oxygen, it may be difficult to reverse the rise in $PaCO_2$ and reduce acidosis without resorting to mechanical ventilation. A stepwise reduction in FiO_2 may be useful in this setting if clinical circumstances permit. An abrupt reduction in FiO_2 is unwise, since it may result in severe hypoxemia.

Definitions

Strength of Recommendation Grading

Grade I: Usually indicated, always acceptable, and considered useful and effective.

Grade IIa: Acceptable, of uncertain effectiveness, and may be controversial. Weight of evidence in favor of usefulness/effectiveness.

Grade IIb: Acceptable, of uncertain effectiveness, and may be controversial. Not well established by evidence, can be helpful, and probably not harmful.

Level of Evidence Grading: (Secondary)

A. Randomized clinical trials (Other clinical studies)
B. Well-designed clinical studies (Clinical studies related to topic but not in this clinical population)
C. Panel consensus (Clinical studies related to topic but not in this clinical population)

Abbreviations

AAT - Alpha1-antitrypsin

ABG - Arterial blood gas

ACLS - Advanced Cardiac Life Support

AECOPD - Acute exacerbation of chronic obstructive pulmonary disease

ASDA - American Sleep Disorders Association (now known as the American Academy of Sleep Medicine)

ATS - American Thoracic Society

BiPAP - Bilevel positive airway pressure

BTS - British Thoracic Society

CABG - Coronary artery bypass graft

COPD - Chronic obstructive pulmonary disease

CPG - Clinical Practice Guideline

CPR - Cardiopulmonary resuscitation

CXR - Chest x-ray

CVA - Cerebrovascular accident

DHHS - Department of Health and Human Services

DoD - Department of Defense

ECG (EKG) - Electrocardiogram

ED - Emergency department

EDS - Excessive daytime sleepiness

ERS - European Respiratory Society

FEV_1 - Forced expiratory volume in one second

FVC - Forced vital capacity

GERD - Gastroesophageal reflux disease

GI - Gastrointestinal

HDIS - High-dose inhaled steroids

Hct - Hematocrit

IPPB - Intermittent positive pressure breathing

ICU - Intensive care unit

LAIBA - Long-acting inhaled beta2-agonists

LTOT - Long-term oxygen therapy

MDI - Metered dose inhaler

MVV - Maximum voluntary ventilation

NC - Nasal cannula

NEB - Nebulizer

NPPV - Noninvasive positive pressure volume

PEEP - Positive end-expiratory pressure

PEF - Peak expiratory flow

PFT - Pulmonary function test

PRN - As needed, whenever necessary

SAIBA - Short-acting inhaled beta2-agonists (LAIBA)

SMZ-TMP - Sulfamethoxazole-trimethoprim

SRT - Sustained-release theophylline

SVN - Small-volume nebulizers

VC - Vital capacity

VHA - Veterans Health Administration

WBC - White blood cell

CLINICAL ALGORITHM(S)

Algorithms are provided for:

Outpatient management of chronic obstructive pulmonary disease

1. Core
2. Acute Exacerbation (A1)
3. Pharmacotherapy (A2)
4. Long-Term Oxygen Therapy (A3)
5. Preoperative Evaluation and Management (A4)
6. Management of Air Travel (A5)
7. Insomnia (A6)

Inpatient management of chronic obstructive pulmonary disease

1. Emergency Room and Hospital Ward (B1)
2. Pharmacotherapy (B2)
3. Oxygen Therapy (B3)

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The algorithm and annotations are based on an exhaustive review of the literature. The goal of the literature review is to provide a systematic basis for the development of an evidence-based guideline. The literature search is followed by critical analysis of the literature, primarily by the clinical experts. To promote an evidence-type approach, the quality of evidence is rated using a hierarchical rating scheme. The value of a hierarchical rating scheme is that it provides a systematic means for evaluating the scientific basis for health care services.

The type of supporting evidence is identified for selected recommendations (see the "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Overall

- The ultimate goal of this guideline is to promote evidence-based management of persons with chronic obstructive pulmonary disease (COPD) and thereby improve clinical outcomes.
- Effective treatment of chronic obstructive pulmonary disease may result in improvement of clinical outcomes.

Specific

Pharmacotherapy

Appropriate use of medications for asthma or chronic obstructive pulmonary disease may alleviate symptoms, increase exercise tolerance, improve pulmonary function, and improve quality of life.

Long-term oxygen therapy

In chronic obstructive pulmonary disease clients with hypoxemia and cor pulmonale, long-term oxygen therapy (LTOT) may increase the life span by 6 to 7 years. Mortality is reduced in patients with chronic hypoxemia when oxygen is administered for more than 12 hours daily and greater survival benefits have been shown with continuous oxygen administration.

Pneumococcal vaccination

Most studies show a benefit, but one small randomized, placebo-controlled trial did not. Case-controlled trials suggest an effectiveness (prevention of pneumococcal infection) of 65 to 84 percent among high-risk patients including those with chronic obstructive pulmonary disease.

Annual influenza vaccination

Influenza vaccination has been shown to be 30 to 80 percent effective in preventing illness, complications, and death in high-risk populations (such as chronic obstructive pulmonary disease).

Smoking cessation

Smoking cessation results in a small improvement in lung function and a slowing of the rate of decline to approximately that seen in never smokers of the same age.

Antibiotic treatment in the patient with acute exacerbation of chronic obstructive pulmonary disease and evidence of respiratory infection

A recent meta-analysis of nine randomized, placebo-controlled studies suggest a small benefit from antibiotic treatment. Antibiotic therapy may be of greater importance in preventing deterioration rather than expediting improvement in outpatients with chronic obstructive pulmonary disease exacerbation. Mild chronic obstructive pulmonary disease exacerbations may not benefit from antibiotics.

Subgroups Most Likely to Benefit:

Antibiotic treatment in the patient with acute exacerbation of chronic obstructive pulmonary disease (COPD) and evidence of respiratory infection

- Older patients, those with a more severe chronic obstructive pulmonary disease and exacerbations featured by increased purulent sputum production are more likely to benefit from antibiotic treatment.

Maximum doses of shorting-acting inhaled beta 2 agonists (SAIBA) and inhaled anticholinergics (IAC) in patients with acute exacerbations of chronic obstructive pulmonary disease

- The combination therapy is especially significant in unmonitored patients in whom there may be concern about toxicity from high-dose SAIBA.

POTENTIAL HARMS

Short-acting inhaled beta2-agonists (SAIBA)

- Inhaled beta2-agonists may cause tremor, increased heart rate, insomnia, restlessness, hypokalemia, or a paradoxical reduction in arterial oxygenation.

Inhaled anticholinergic agent (i.e., ipratropium)

- Inhaled ipratropium may cause dry mouth or increased heart rate, or exacerbate glaucoma, benign prostatic hypertrophy or other conditions potentially worsened by the drug's anti-cholinergic activity.

Steroids, oral and inhaled

- Adverse effects of oral corticosteroids are numerous and include: hypertension, hyperglycemia, weight gain, immunosuppression, skin thinning, personality, purpura, mental status changes, depression, glaucoma, cataracts, and adrenal suppression. Patients requiring long-term steroids should be evaluated for risk of osteoporosis and preventive measures instituted, such as calcium and vitamin D supplements, weight-bearing exercise and hormone replacement therapy if appropriate.
- Adverse effects of inhaled corticosteroids include oral candidiasis, hoarseness, and possible adrenal suppression at high doses.

Theophylline

- Theophylline has a narrow therapeutic index, with the potential for dose related adverse reactions that include insomnia, anxiety, nausea, vomiting, tremor, arrhythmias, delirium, seizures, and death.
- Attempts to withdraw theophylline, even at lower levels, should be done cautiously, since deterioration in pulmonary function and exercise performance may occur.

Subgroups Most Likely to be Harmed:

Caution should be taken when maximal doses of short-acting inhaled beta2-agonists (SAIBA) or when systemic (injected) beta2-agonists (e.g., epinephrine) are given to patients with known coronary artery disease, left ventricular dysfunction, or history of arrhythmia.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The reader is reminded that this document is intended as a guideline and accordingly, should not supersede the clinical judgment of the healthcare provider.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Veterans Health Administration (VHA). Clinical practice guideline for the management of chronic obstructive pulmonary disease. Version 1.1a. Washington (DC): Department of Veterans Affairs (U.S.), Veterans Health Administration; 1999 Aug. 116 p.

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999 Aug

GUIDELINE DEVELOPER(S)

Department of Defense - Federal Government Agency [U.S.]
Veterans Health Administration - Federal Government Agency [U.S.]

SOURCE(S) OF FUNDING

United States Government

GUIDELINE COMMITTEE

Chronic Obstructive Pulmonary Disease Workgroup

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Working Group Members: Peter Almenoff, MD; Gregg Anders, LTC, MC, USAF; Teresa Bisnett, Maj, MC, USA; John Brown, LCDR, MC, USN; John Christman, MD; Barry Cusack, MD; Donald W. Degroff, Maj, MSC, USA; Thomas Dillard, Col, MC, USA; Alan Fein, MD; Thomas Fraser, Capt, MC, USAF; Maqual Infranca Graham, PharmD; Nicholas Gross, MD, PhD; Michael Habib, MD; Wayne T. Honeycutt, LTC, MC, USA; David Hudgel, MD; Kenneth Hurwitz, Maj, MC, USA; Michael Krafczyk, Capt, MC, USA; Michael Littner, MD; Jennifer, Capt, MC, USAF; John P. Mitchell, Lt Col, MC, USAF; Toni Mitchell, MD; Joe Parker, LTC, MC, USA; Luis A. Ramos, LT, MSC, USN; Gordon Snider, MD; Oded Susskind, MPH; Sean Tunis, MD; Joy Williams, RN, RRT, MHA.

Other Participants: JB Aguera-Arcas, MD; Sid Atkinson, Col, MC, USA; Marsha Beaugrand, CDR, MSC, USN; Gerald Cox, CDR, MC, USN; Kathryn J. Dolter, RN, PhD, LTC, AN; Rosalie Fishman, RN, MSN, CPHQ; Sarah Ingersoll, RN; Barbara Jones, RRA; Arthur Kaufman, MD; Genny Drakau; Louise H. Nelson, RN; George

Pickett, MD, MPH; Arnyce Pock, Lt Col, MC, USAF; Janet Spinks, RN, MS, CPHQ; Debby Walder, RN, MSN.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

It updates the guidelines developed in 1997 (Clinical practice guideline for the management of persons with chronic obstructive pulmonary disease. Washington [DC]: Department of Veterans Affairs; 1997. Various pagings).

GUIDELINE AVAILABILITY

Electronic copies: Available from the Department of Veterans Affairs Web site.

Print copies: Department of Veterans Affairs, Veterans Health Administration, Office of Quality and Performance (10Q) 810 Vermont Ave. NW, Washington, DC 20420.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- The pharmacologic management of chronic obstructive pulmonary disease. Supplement to the VHA/DoD clinical practice guideline for the management of chronic obstructive pulmonary disease. Washington (DC): Veterans Health Administration Pharmacy Benefits Management Strategic Healthcare Group, 1999 Jun. 42 p.

Electronic copies: Veterans Health Administration Pharmacy Benefits Management Web site.

Print copies: Veterans Health Administration, Department of Veterans Affairs, 50 Irving St, SW, Washington, DC 20422.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on September 9, 1999. The information was verified by the guideline developer on January 10, 2000. The summary was updated by ECRI on May 6, 2001.

COPYRIGHT STATEMENT

Date Modified: 4/12/2004